Supplementary Information

Design, Synthesis and Bioactivity Studies of Novel Triazolopyrimidinone Compounds

Huseyin Istanbullu,[*,1] Gulsah Bayraktar,[2] Ismail Ozturk,[3] Gunes Coban,[2] Merve Saylam[1]
[1]*Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Izmir Katip Celebi University, Izmir, Turkey:*
[2]*Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Ege University, Izmir, Turkey: and*
[3]*Department of Pharmaceutical Microbiology, Faculty of Pharmacy, Izmir Katip Celebi University, Izmir, Turkey.*

[*] Correspondence e-mail: huseyin.istanbullu@ikc.edu.tr

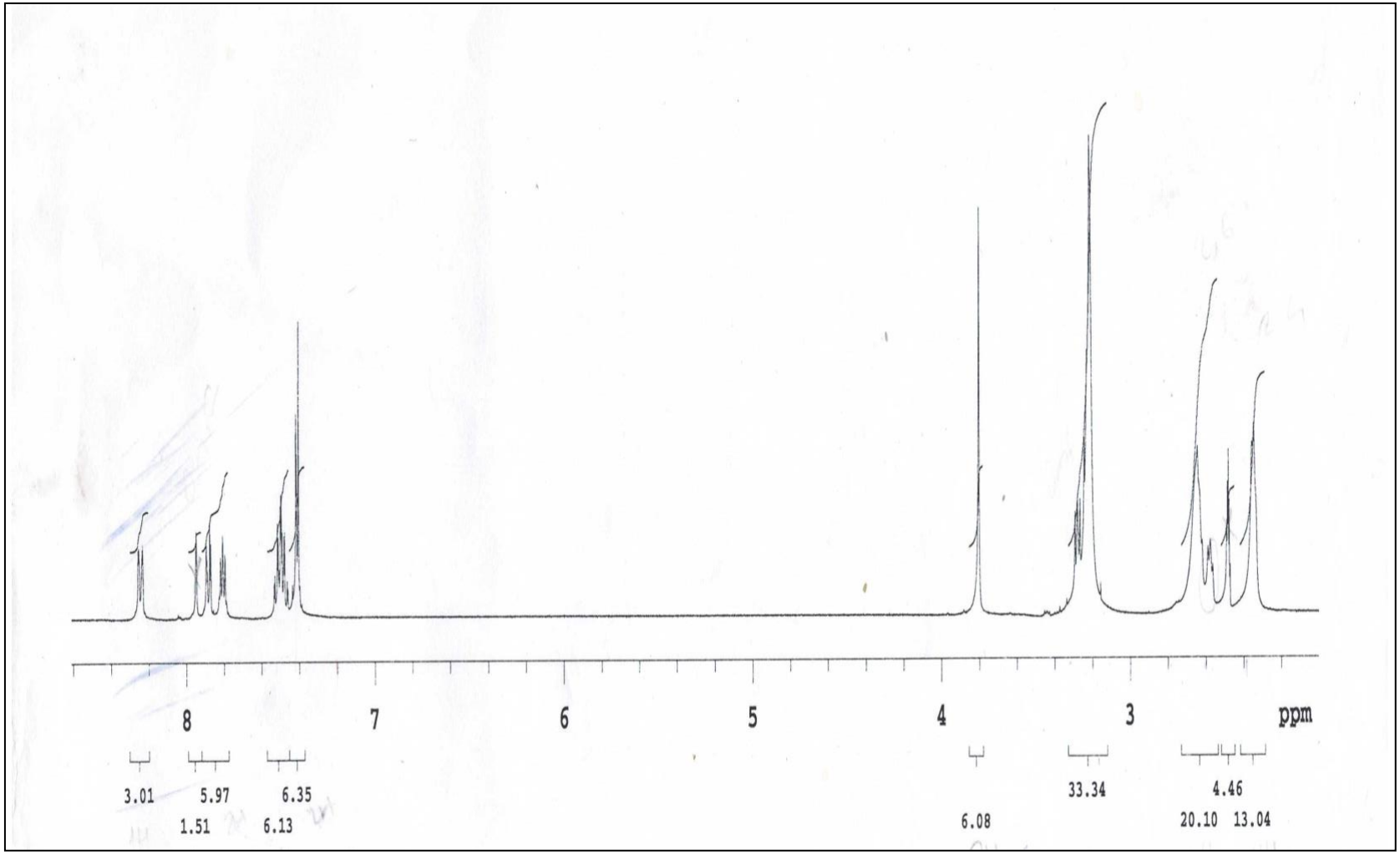


Figure S1. ^{1}H NMR spectra of NMP

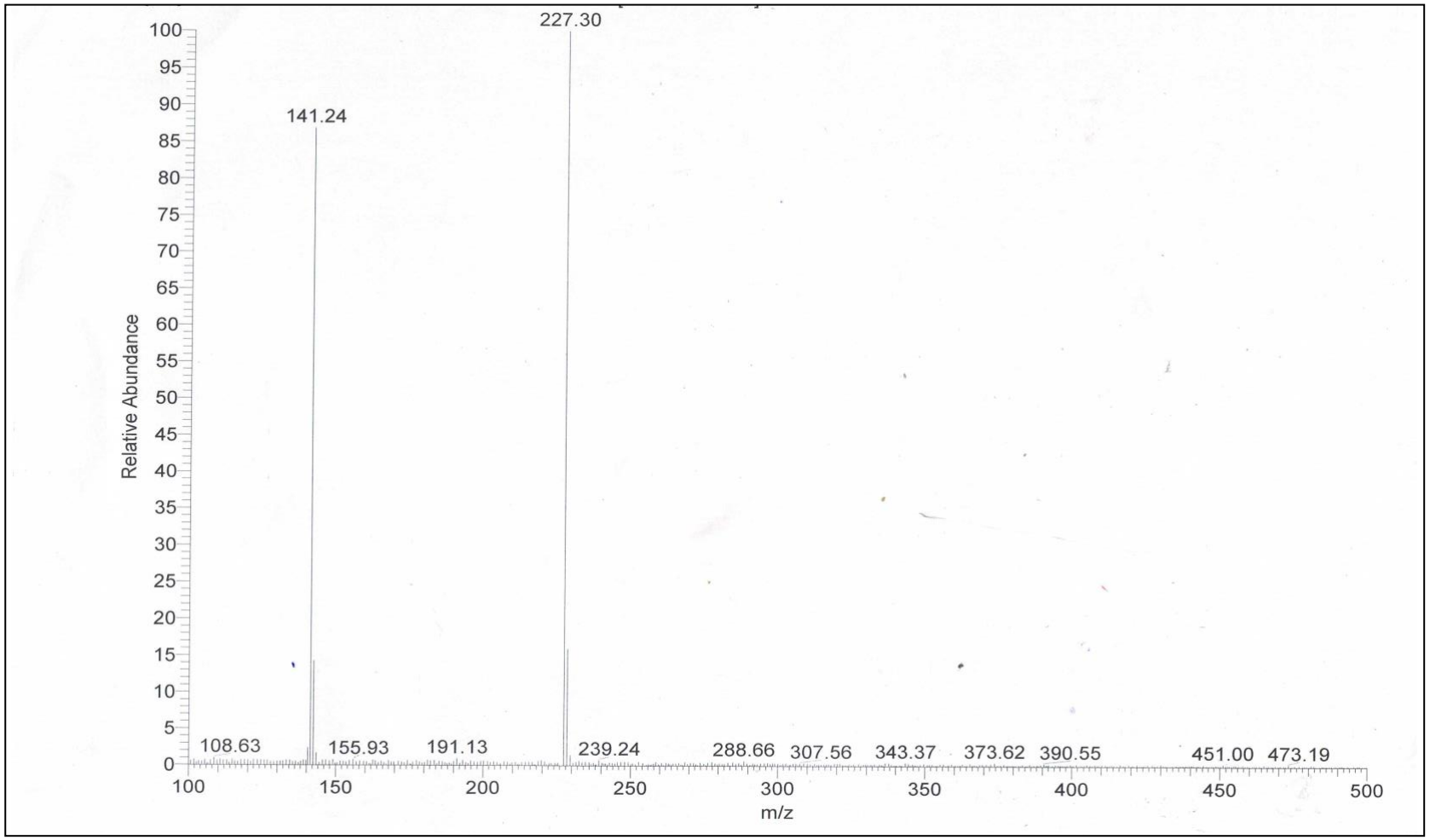


Figure S2. Mass spectra of NMP

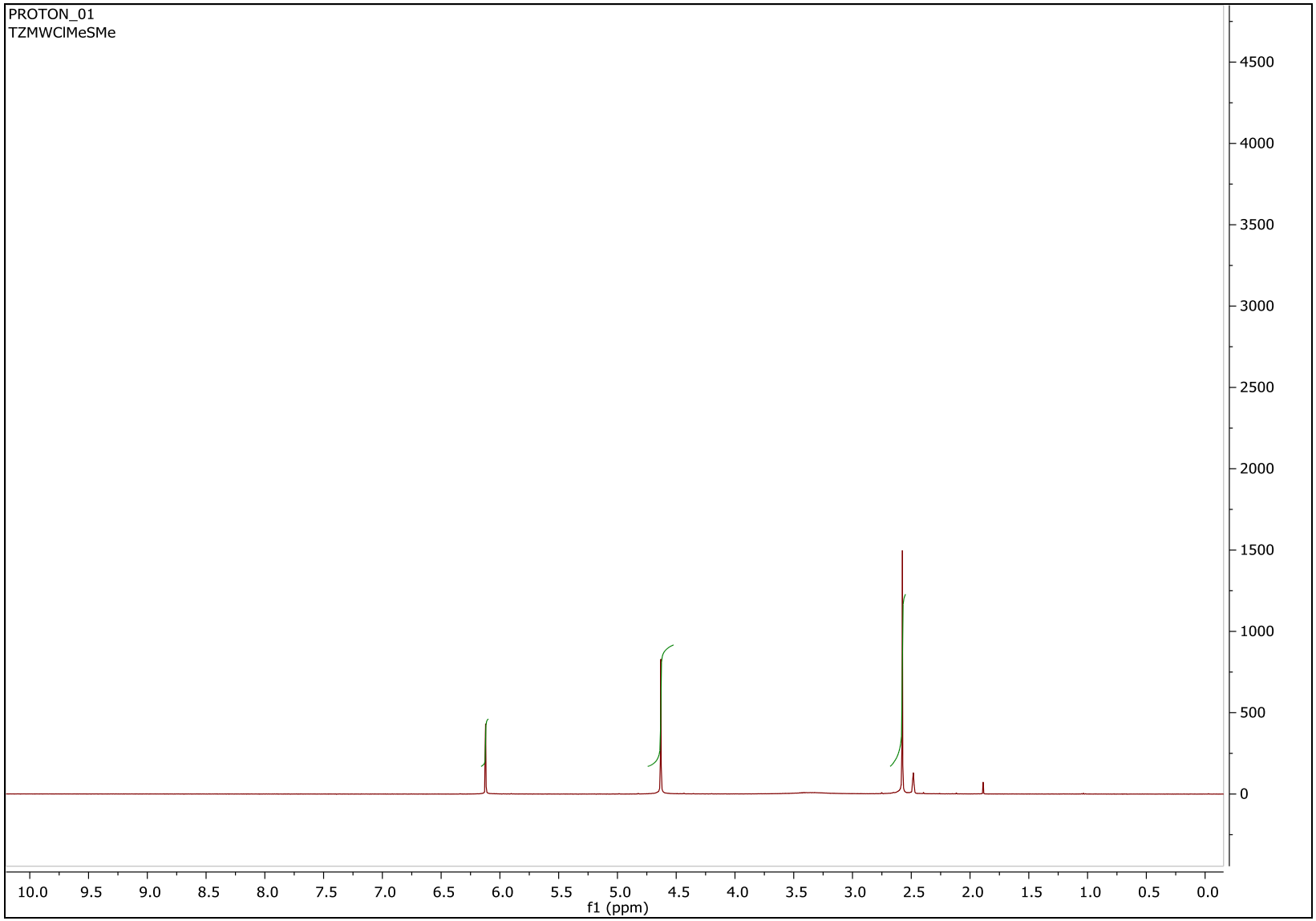


Figure S3. ^{1}H NMR spectra of TP1

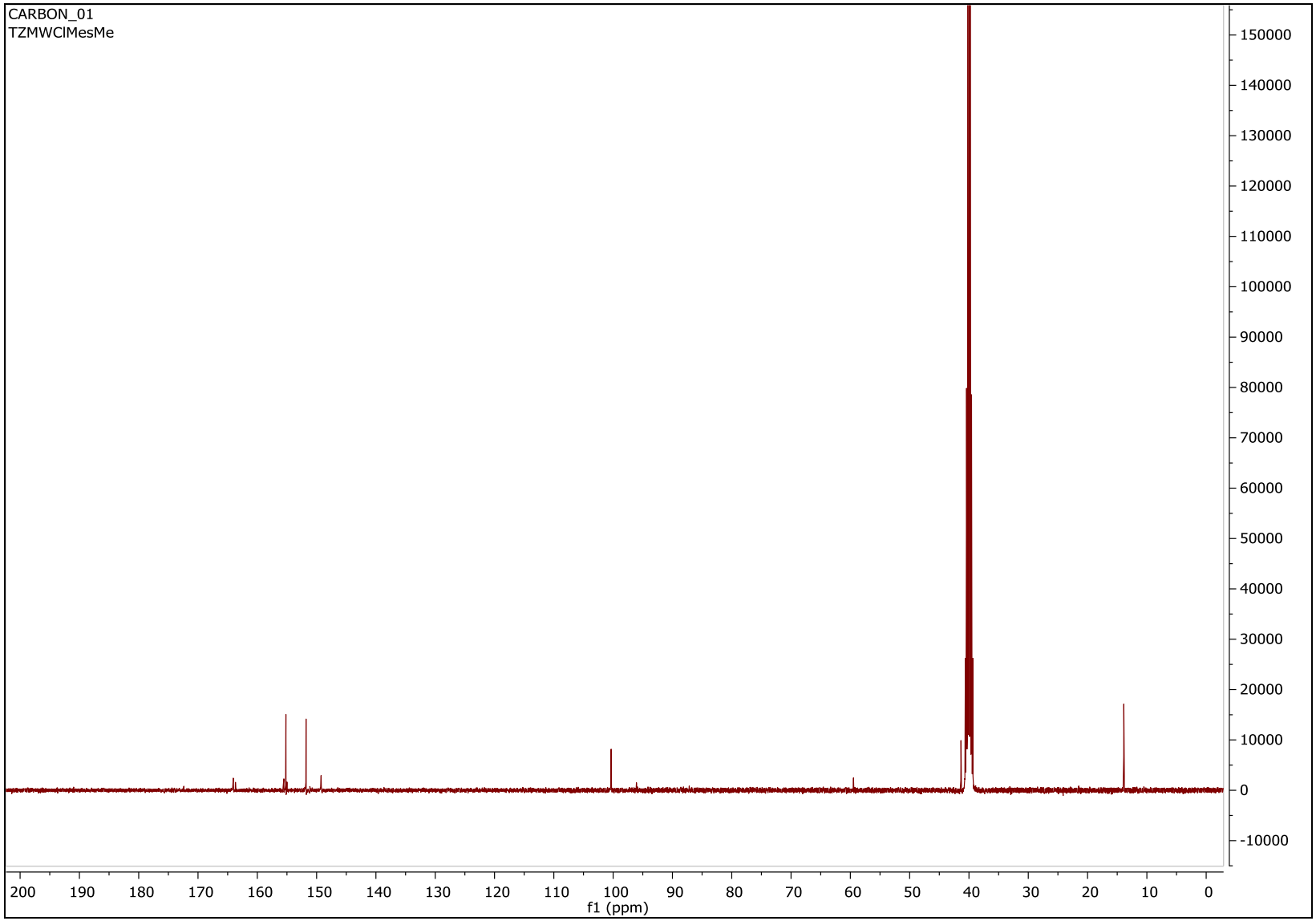


Figure S4. ^{13}C NMR spectra of TP1

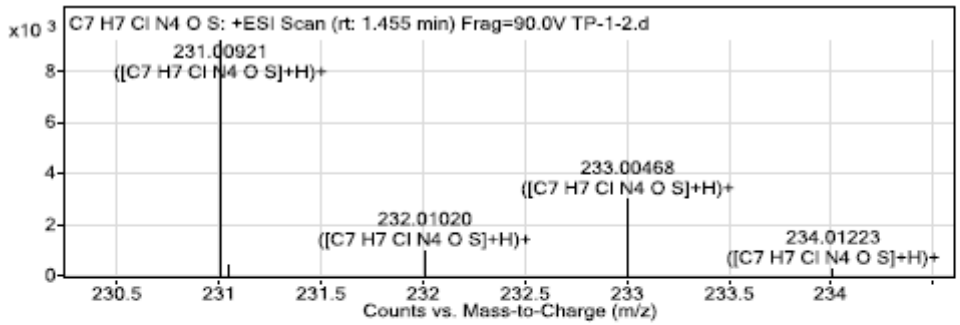
Qualitative Analysis Report

Data Filename	TP-1-2.d	**Sample Name**	TP-1-2
Sample Type	Sample	**Position**	P1-D4
Instrument Name	Instrument 1	**User Name**	OGUZHAN DALKILIC
Acq Method	ESI pos.m	**Acquired Time**	8/17/2021 5:38:43 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.08.00 (B8058.0)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
90	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
102.12636	1	38473.24		
102.15576		1521.84		
102.2152		907.6		
102.23997		514.02		
103.12866	1	2520.62		
115.10911		1703.71		
118.08392		383.4		
139.04905		425.96		
144.97946		644.9		
146.97801		425.29		
157.03355		506.63		
163.13008		1089		
173.04731		678.53		
173.15258		496.97		
185.11372		531.96		
191.16212	1	6333.54		
191.1952		362.45		
192.16523	1	508.88		
194.11494		429.06		
194.15149		592.27		
208.18904		383.39		
213.14297	1	4444.17		
214.14729	1	380.53		

Figure S5. HRMS Qualitative analaysis of TP1

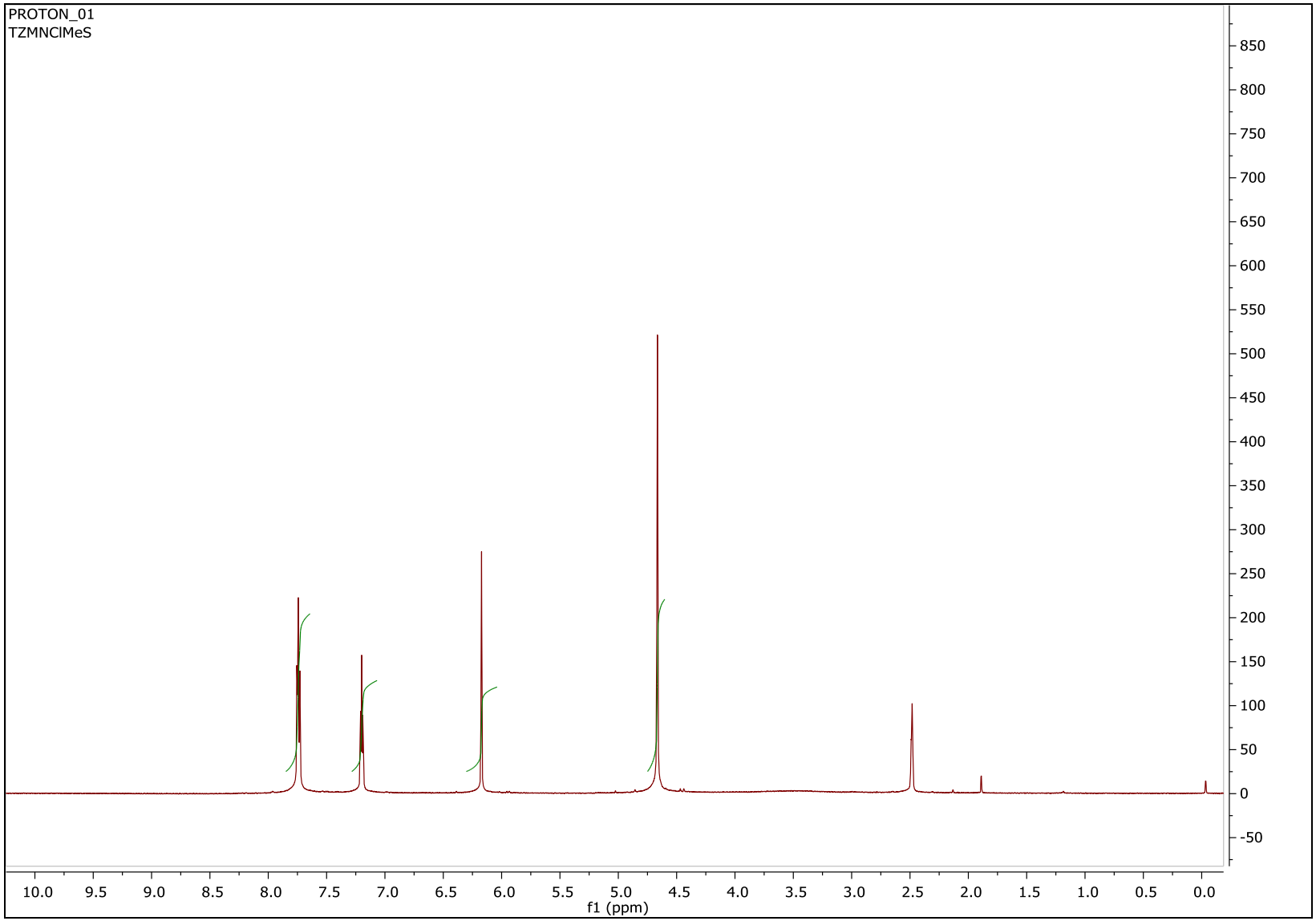


Figure S6. ^{1}H NMR spectra of TP2

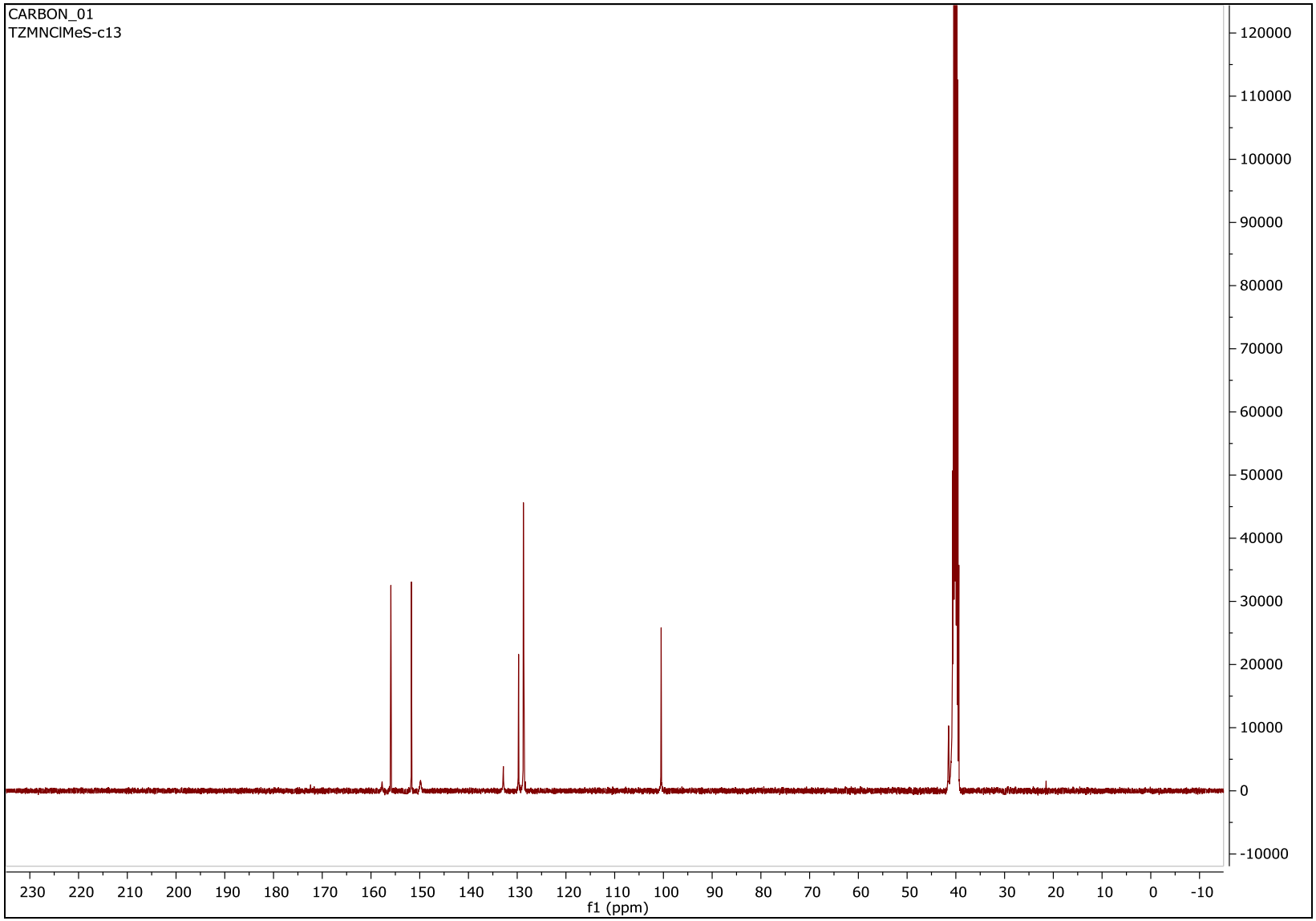


Figure S7. ^{13}C NMR spectra of TP2

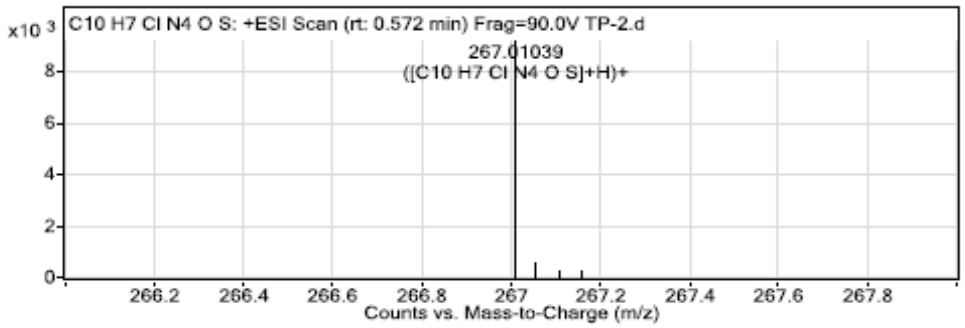
Qualitative Analysis Report

Data Filename	TP-2.d	**Sample Name**	TP-2
Sample Type	Sample	**Position**	P1-D5
Instrument Name	Instrument 1	**User Name**	OGUZHAN DALKILIC
Acq Method	ESI pos.m	**Acquired Time**	8/17/2021 5:41:25 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.08.00 (B8058.0)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
90	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
102.12631	1	28826.01		
102.15439		1097.33		
102.21597		610.09		
103.12978	1	1689.47		
105.04015		454.66		
115.11057		1035.96		
122.05527		368.4		
144.98051		732.07		
157.03238		2319.09		
163.13028		398.99		
173.04758		408.4		
173.07815		375.72		
185.1128		615.17		
191.16147		2436.89		
194.11715		493.72		
194.15118		614.41		
207.15652		514.38		
213.14384	1	3085.74		
215.1247		669.21		
224.12556		1394.86		
225.00477		381.15		
228.19148		424.31		
230.24769		665.07		

Figure S8. HRMS Qualitative analaysis of TP2

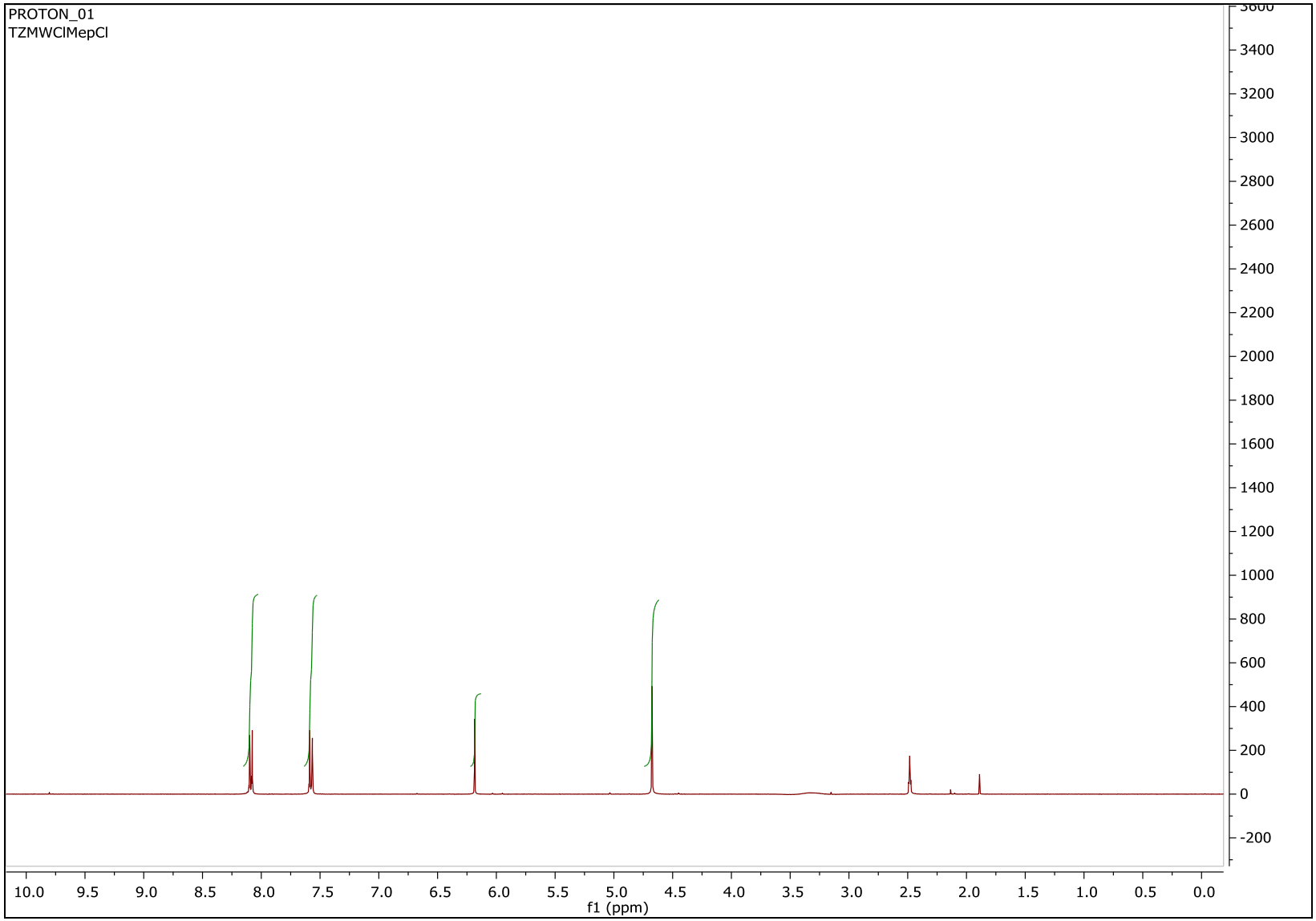


Figure S9. ^{1}H NMR spectra of TP3

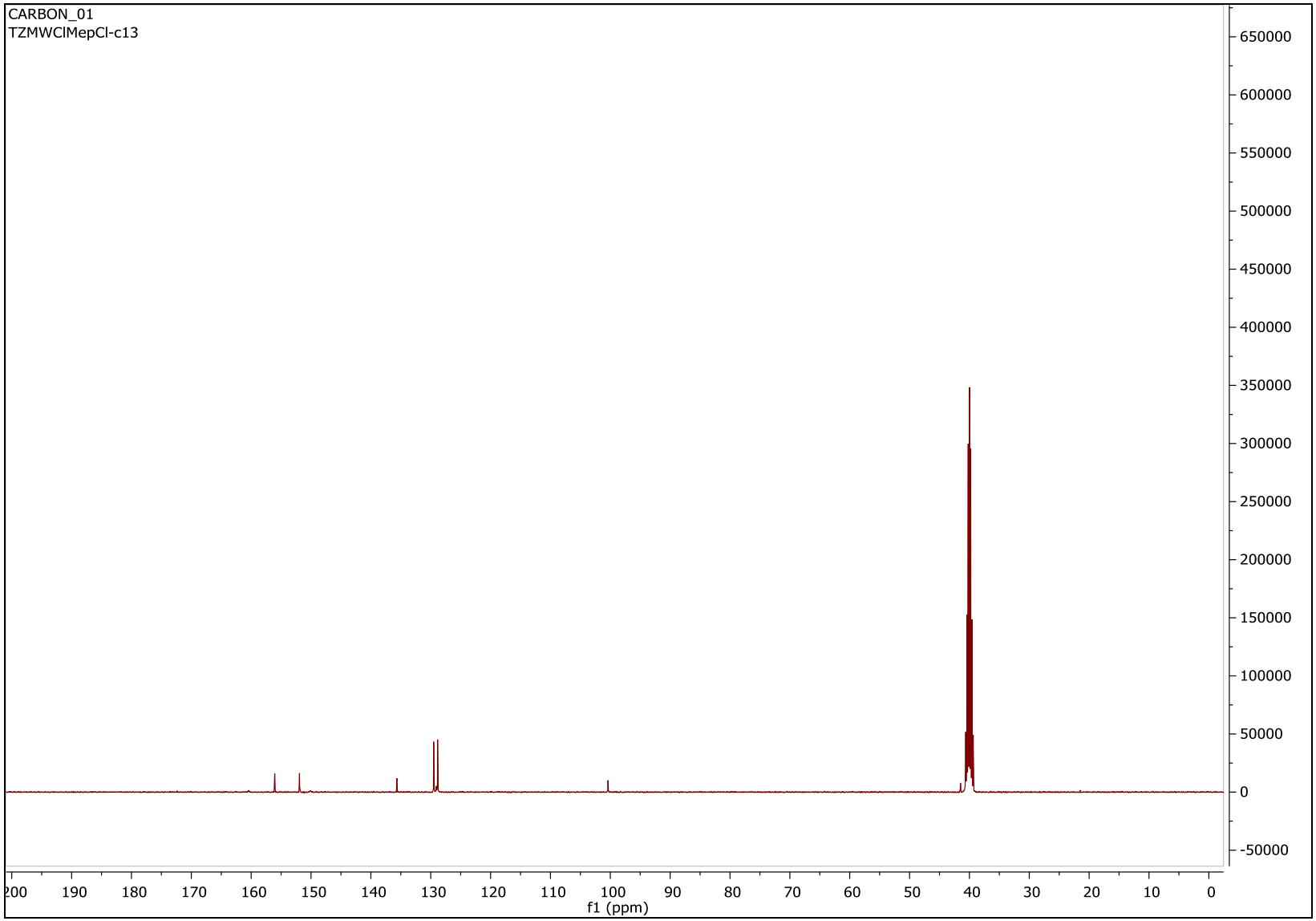


Figure S10. ^{13}C NMR spectra of TP3

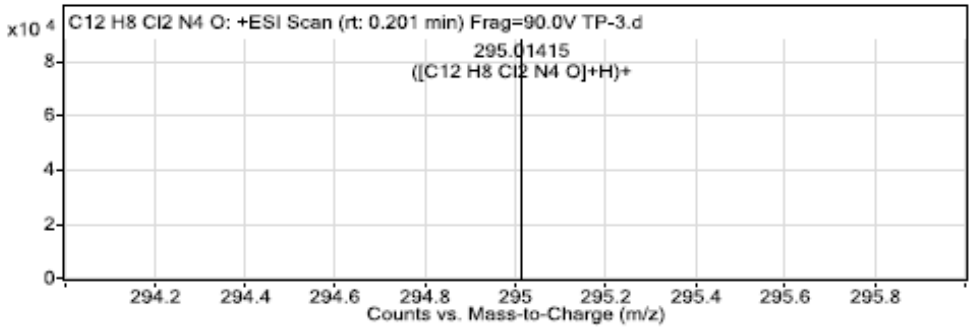
Qualitative Analysis Report

Data Filename	TP-3.d	**Sample Name**	TP-3
Sample Type	Sample	**Position**	P1-D6
Instrument Name	Instrument 1	**User Name**	OGUZHAN DALKILIC
Acq Method	ESI pos.m	**Acquired Time**	8/17/2021 5:44:07 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.08.00 (B8058.0)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
90	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
102.12698		1200.68		
157.03323	1	10150.09		
158.03578	1	950.89		
159.02858	1	1111.68		
195.0416	1	7802.76		
197.03905	1	2636.64		
233.05723		1384.43		
237.053	1	5937.71		
239.04992	1	2014.34		
251.06741	1	3362.4		
253.06333	1	1271.74		
274.27264	1	3731.88		
295.01415	1	87463.24	C12 H8 Cl2 N4 O	(M+H)+
296.01723	1	11027.06	C12 H8 Cl2 N4 O	(M+H)+
297.01105	1	56467.62	C12 H8 Cl2 N4 O	(M+H)+
297.0636	1	2381.65		
297.15975		1424.34		
298.01321	1	6620.41	C12 H8 Cl2 N4 O	(M+H)+
299.0079	1	8158.75	C12 H8 Cl2 N4 O	(M+H)+
300.00925	1	880.84	C12 H8 Cl2 N4 O	(M+H)+
302.30568		861.6		
305.07747	1	2053.72		
307.0827	1	901.57		

Figure S11. HRMS Qualitative analysis of TP3

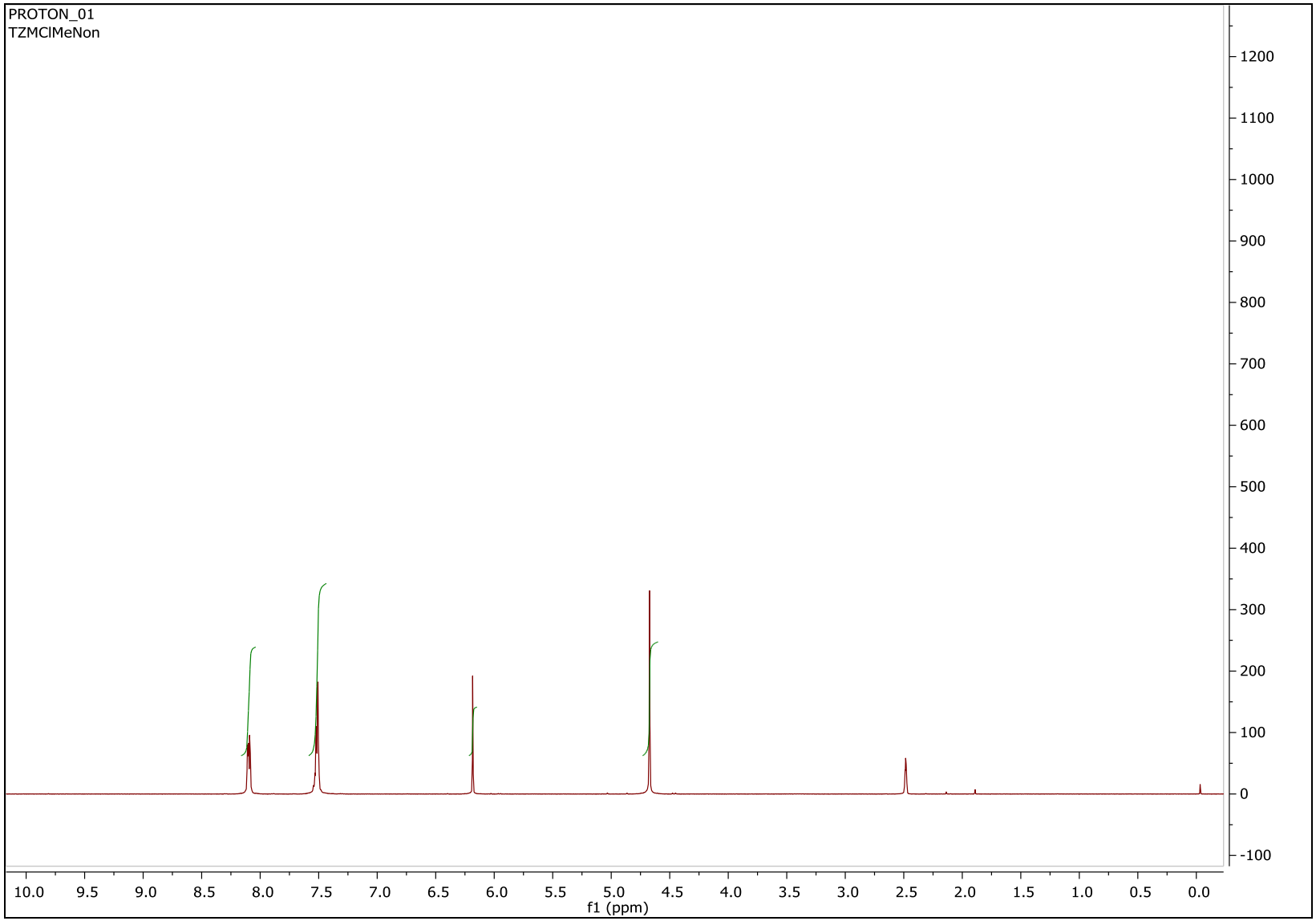


Figure S12. ^{1}H NMR spectra of TP4

Figure S13. ^{13}C NMR spectra of TP4

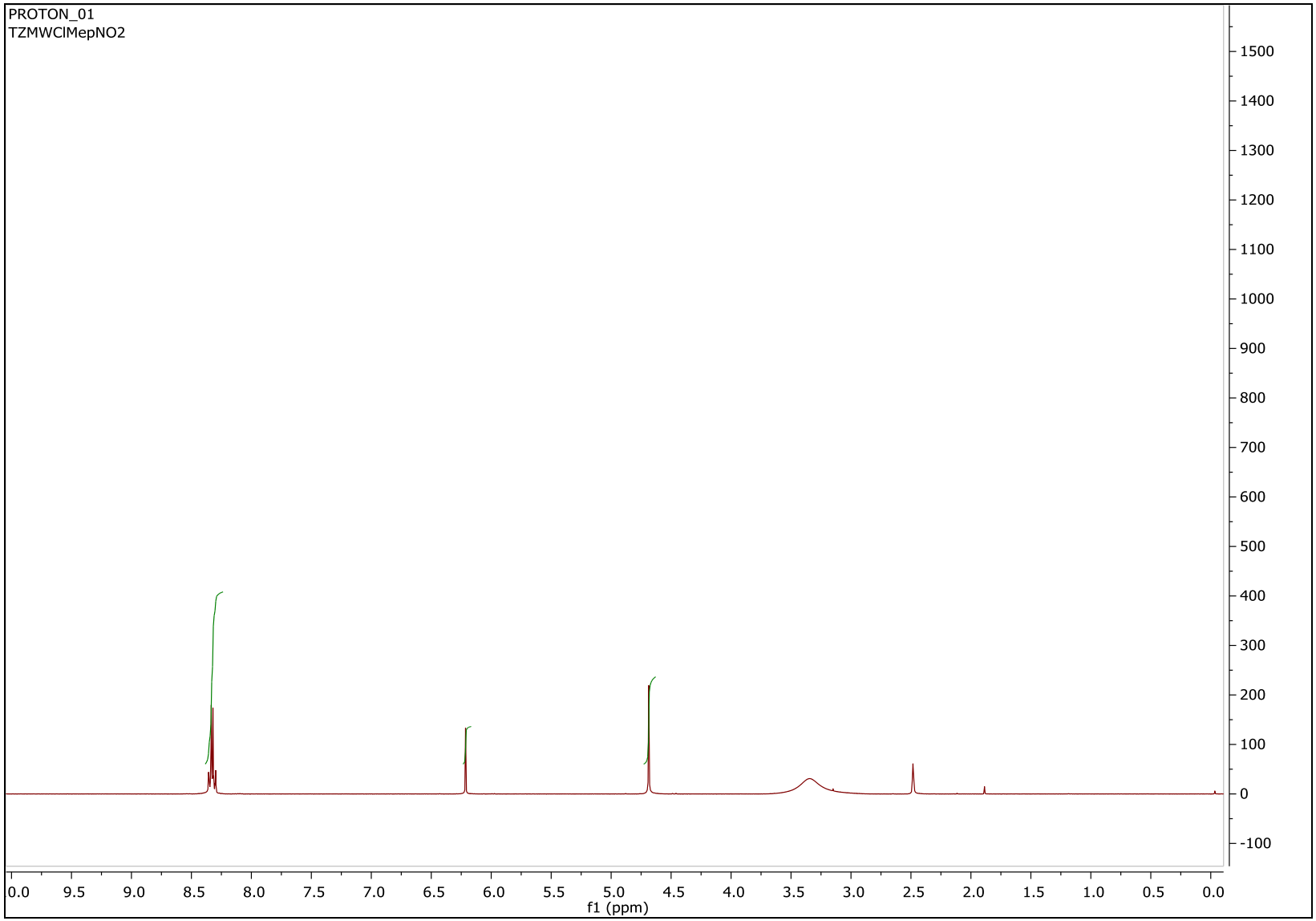


Figure S14. ^{1}H NMR spectra of TP5

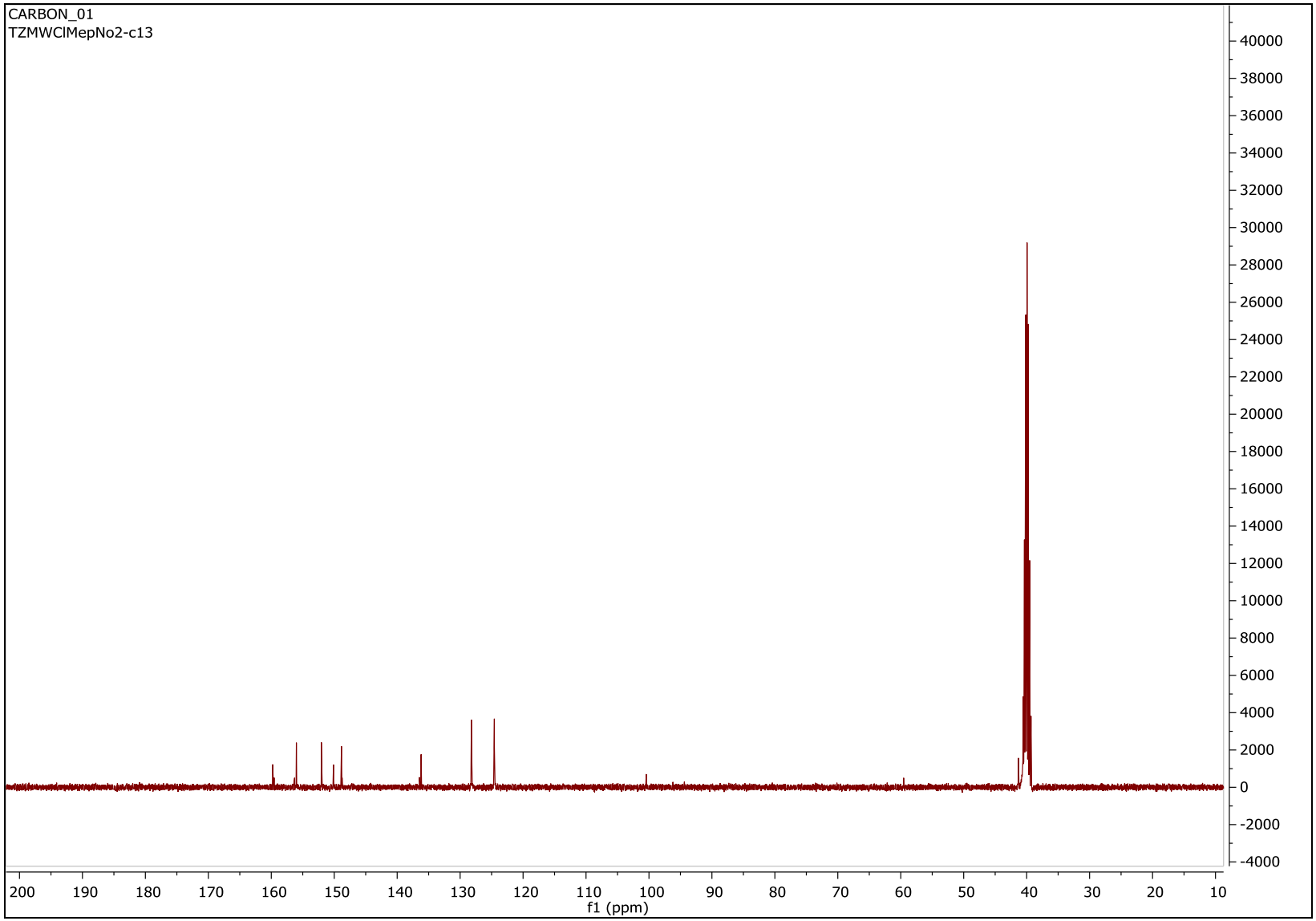


Figure S15. ^{13}C NMR spectra of TP5

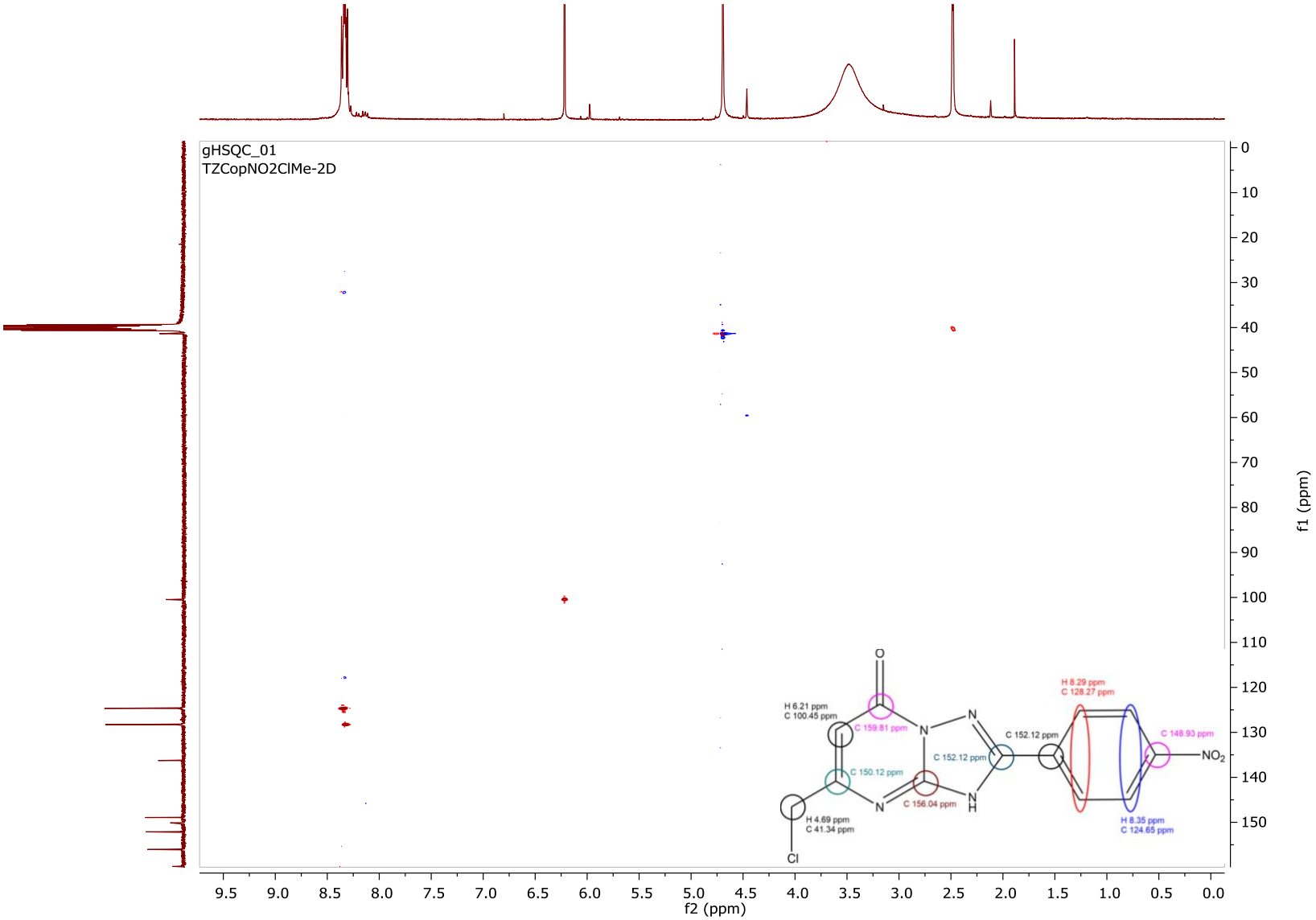


Figure S16. HSQC NMR spectra of TP5

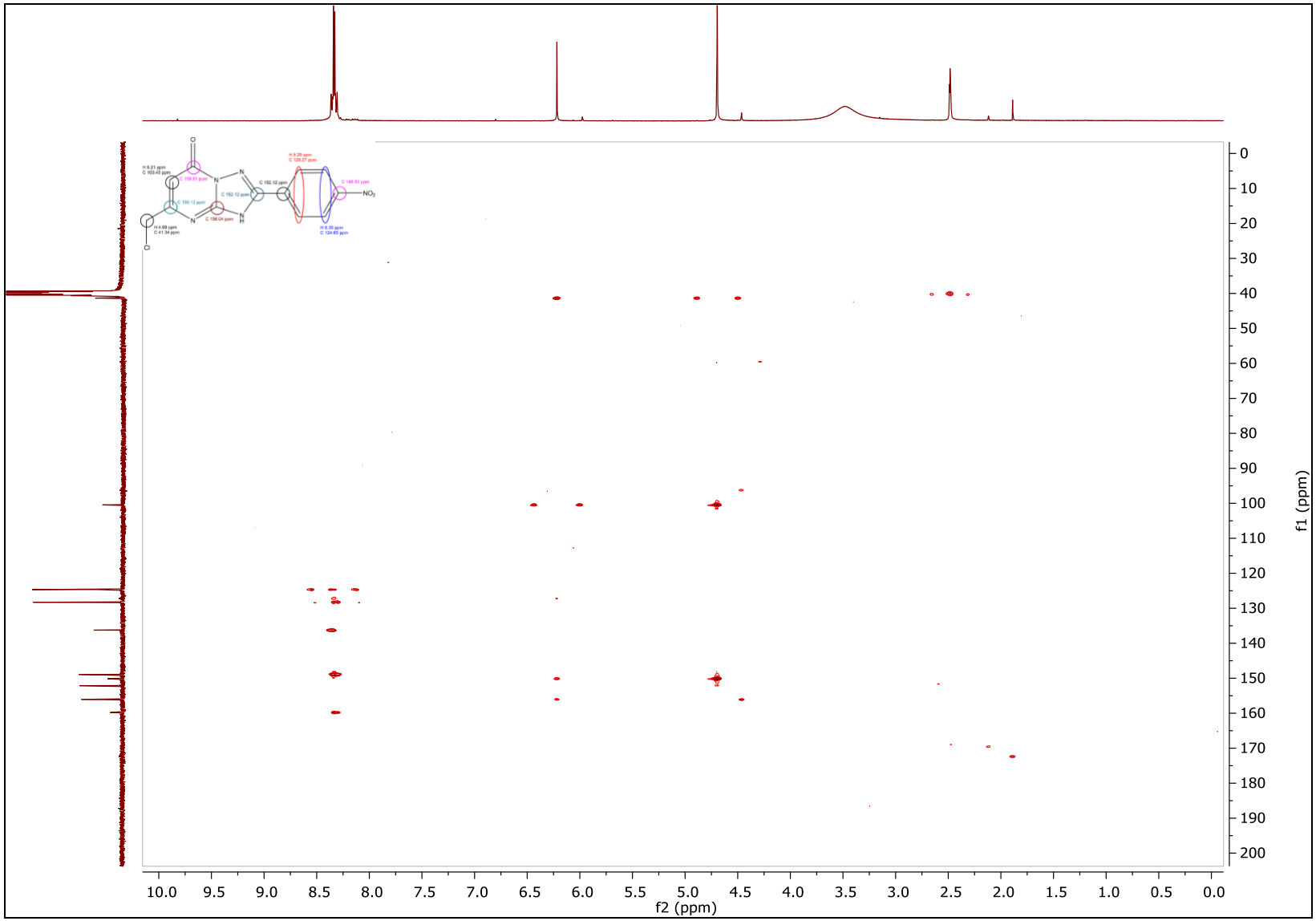


Figure S17. HMBC NMR spectra of TP5

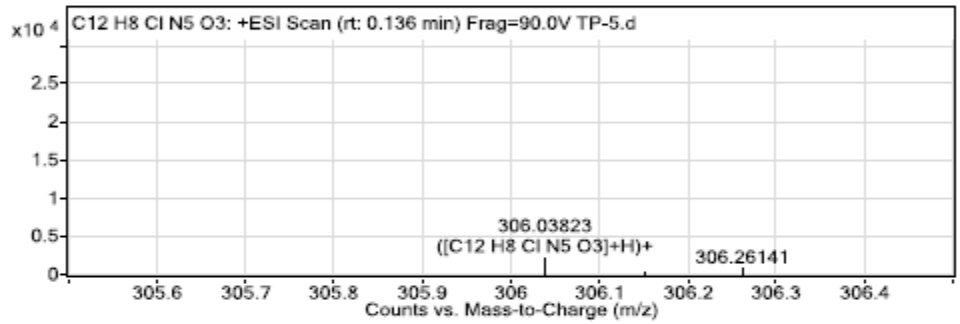
Qualitative Analysis Report

Data Filename	TP-5.d	**Sample Name**	TP-5
Sample Type	Sample	**Position**	P1-D7
Instrument Name	Instrument 1	**User Name**	OGUZHAN DALKILIC
Acq Method	ESI pos.m	**Acquired Time**	8/17/2021 5:46:49 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.08.00 (B8058.0)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
90	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
101.00183		3719.1		
102.12658	1	6113.2		
157.03358	1	25113.7		
157.07148		1132.72		
158.03493	1	1111		
159.02974	1	1756.03		
206.06525		1841.93		
218.20847		2470.22		
230.24659		2983		
239.14787		893.75		
246.24086	1	2173.65		
258.2767		1261.05		
262.23457		1979.93		
274.27284	1	25469.35		
274.31575		1452.04		
275.2761	1	3923.41		
288.28655		1982.98		
290.26618		1634.24		
300.19938	1	2254.28		
302.30284	1	3543.01		
306.03823	1	2225.11	C12 H8 Cl N5 O3	(M+H)+
316.32121		1347.12		
318.2986	1	26382.62		

Figure S18. HRMS Qualitative analysis of TP5

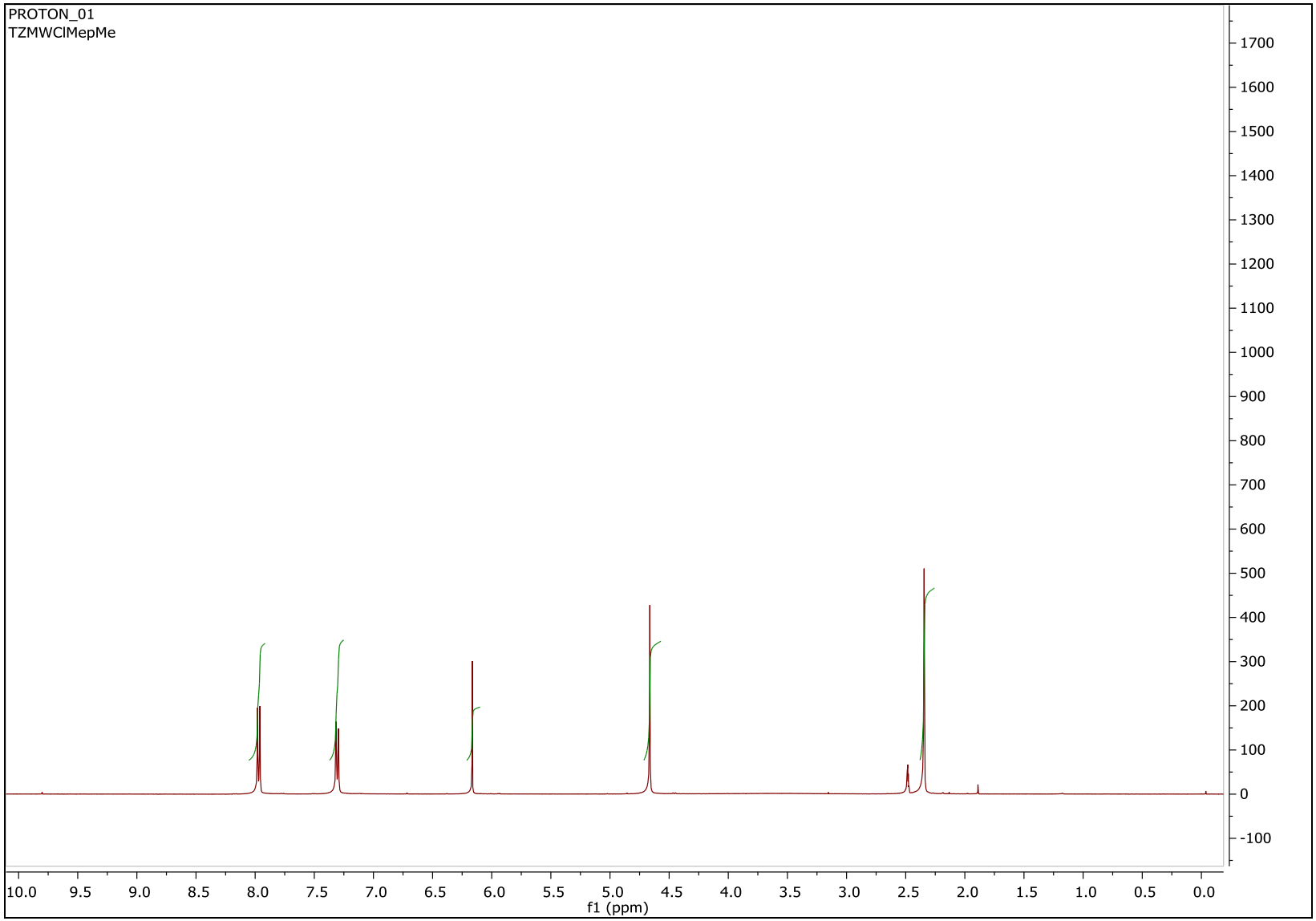


Figure S19. ^{1}H NMR spectra of TP6

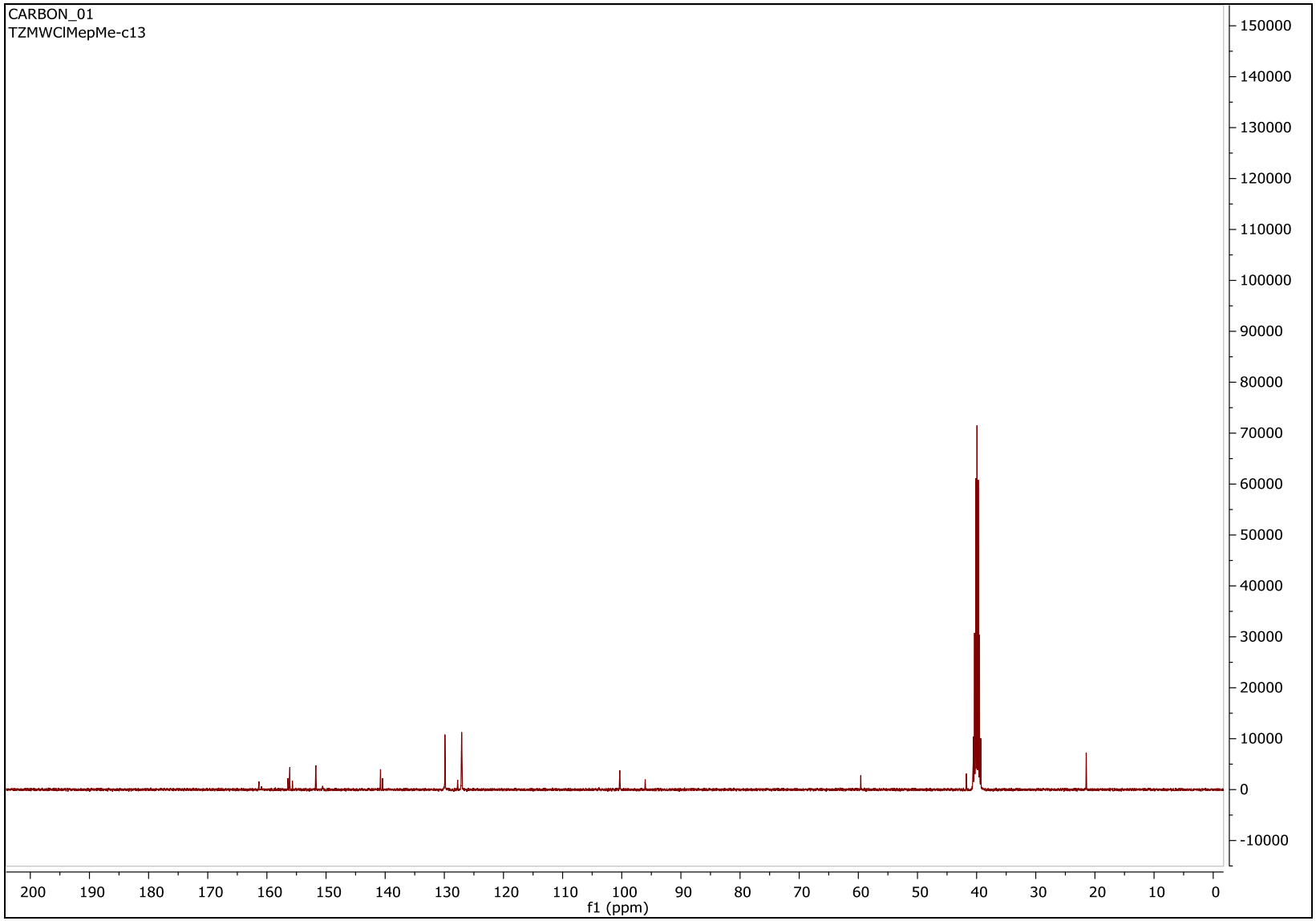


Figure S20. ^{13}C NMR spectra of TP6

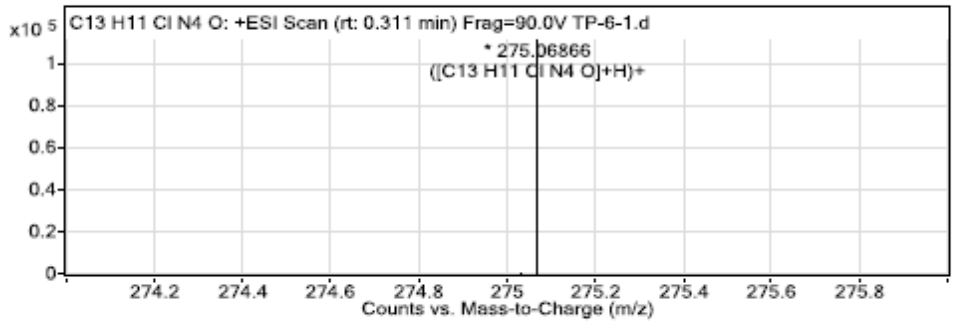
Qualitative Analysis Report

Data Filename	TP-6-1.d	**Sample Name**	TP-6-1
Sample Type	Sample	**Position**	P1-D8
Instrument Name	Instrument 1	**User Name**	OGUZHAN DALKILIC
Acq Method	ESI pos.m	**Acquired Time**	8/17/2021 5:49:31 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.08.00 (B8058.0)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
90	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
102.12656	1	14990.29		
102.15127		939.81		
103.12923	1	1444.61		
157.03398		4276.28		
224.12705		923.6		
230.24398		1054.82		
275.06866	1	111064.66	C13 H11 Cl N4 O	(M+H)+
276.07065	1	13922.09	C13 H11 Cl N4 O	(M+H)+
276.12027		809.24		
277.06555	1	30550.48	C13 H11 Cl N4 O	(M+H)+
277.10921		1640.94		
278.06785	1	4524.11		
284.32986		1138.49		
297.0505	1	60191.68		
297.20031		1181.8		
298.05352	1	7454.82		
298.14333		1469.87		
299.04707	1	17142.33		
299.10898		2569.44		
299.14592		934.66		
300.04988		2246.3		
306.11018		911.65		
313.02462	1	14101.4		

Figure S21. HRMS Qualitative analysis of TP6

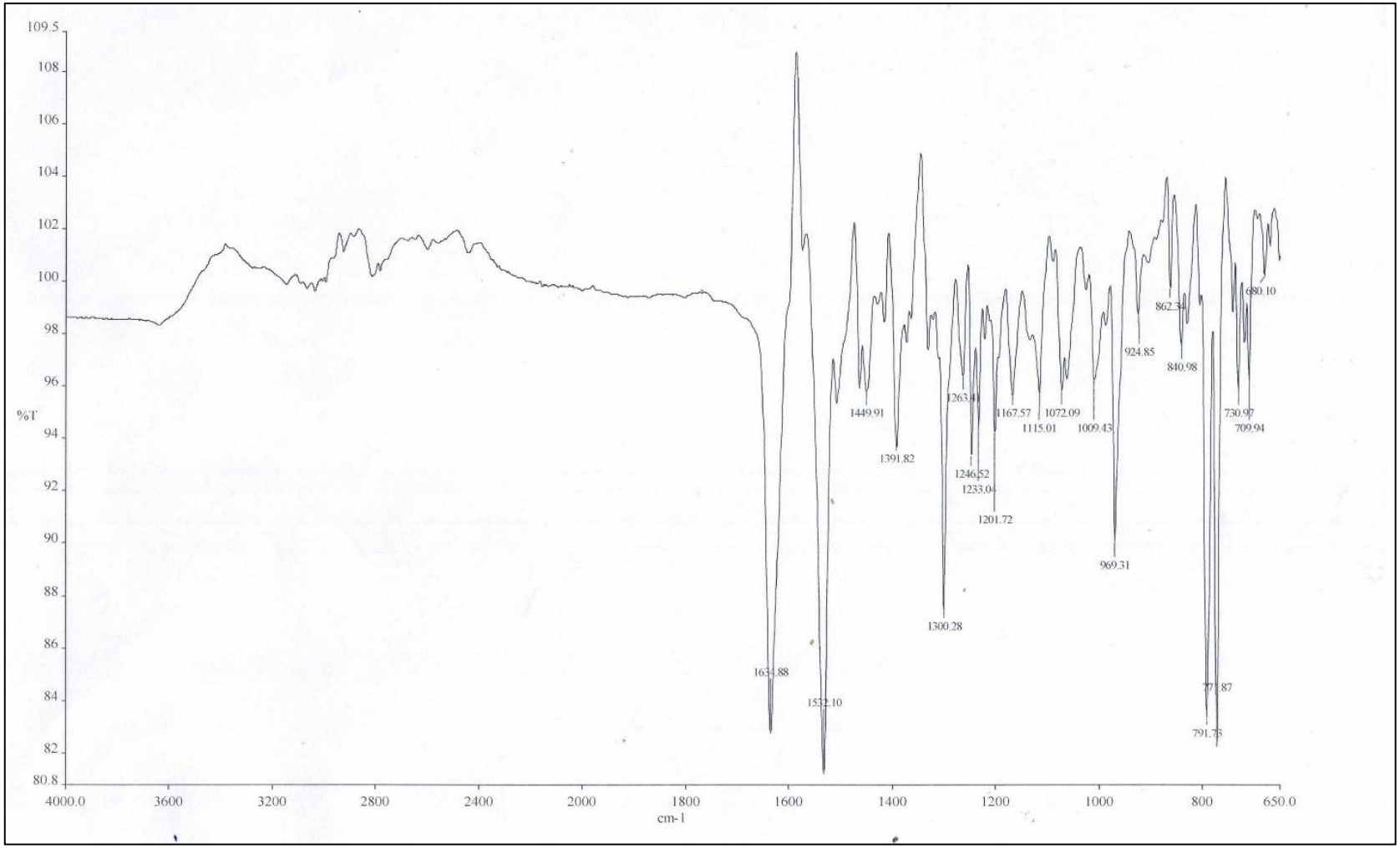


Figure S22. IR Spectra of H1

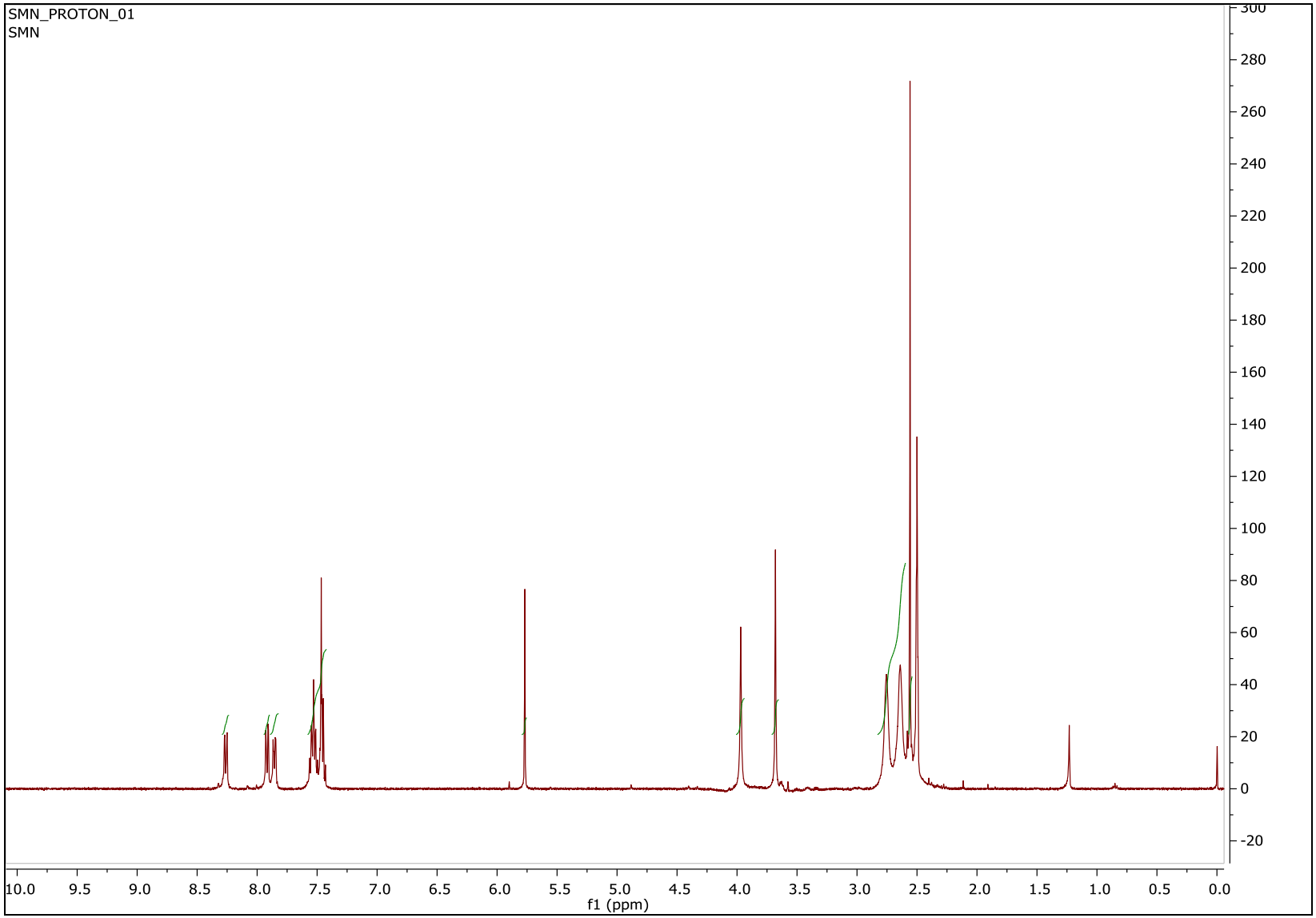


Figure S23. ^{1}H NMR Spectra of H1

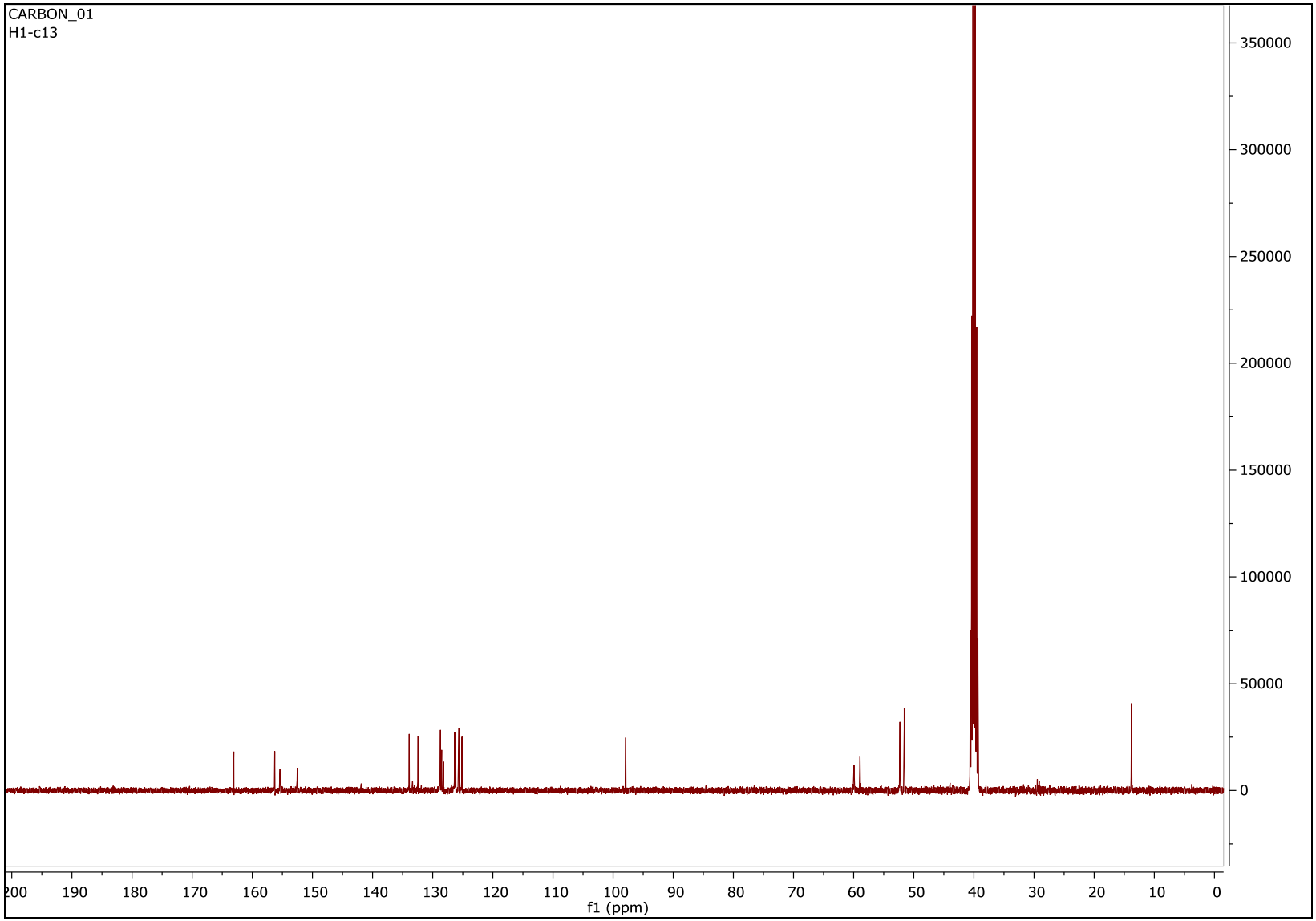


Figure S24. ^{13}C NMR Spectra of H1

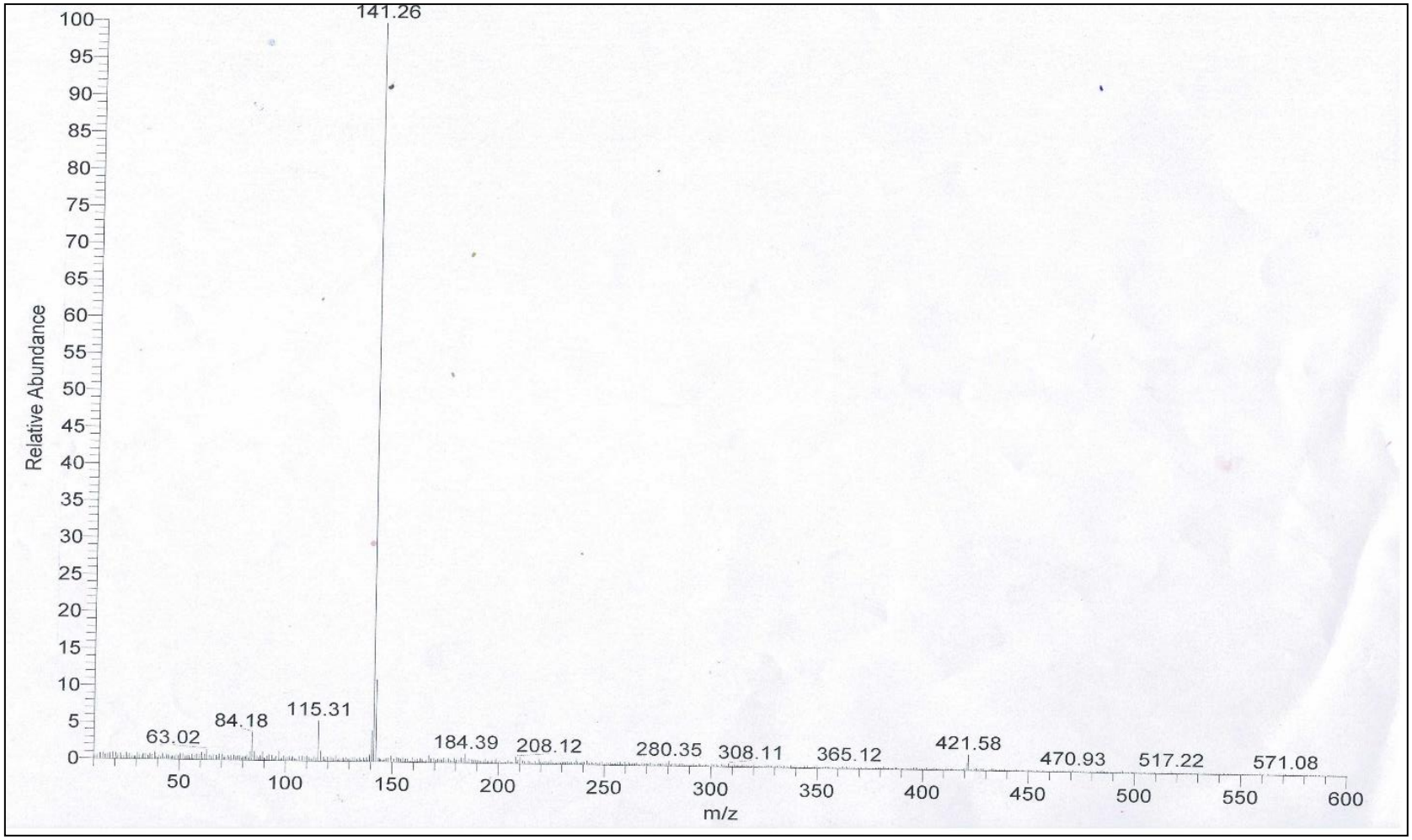


Figure S25. Mass Spectra of H1

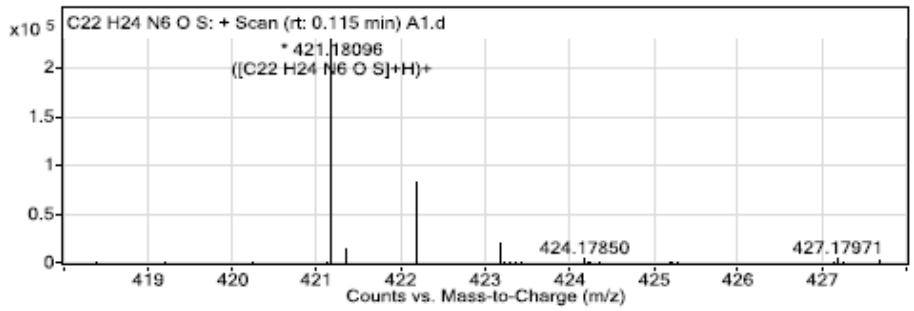
Qualitative Analysis Report

Data Filename	A1.d	**Sample Name**	A1
Sample Type	Sample	**Position**	P1-C2
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI pos.m	**Acquired Time**	2/17/2020 3:37:58 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.08.00 (B8058.0)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
90	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
121.04963	1	22154.42		
141.06881	1	15221.89		
241.16871	1	23480.19		
281.11605	1	13618.8		
293.17378	1	14500.09		
421.18096	1	228842.94	C22 H24 N6 O S	(M+H)+
421.35678		14063.17		
422.18255	1	82561.04	C22 H24 N6 O S	(M+H)+
423.18037	1	21108.69	C22 H24 N6 O S	(M+H)+
449.26853	1	36411.75		
450.27047	1	10373.82		
659.32485	1	14402.02		
661.34062	1	23178.86		
662.34591	1	10818.57		
841.35581	1	229141.3		
842.35762	1	153131.27		
843.35515	1	61593.79		
844.35602	1	15560.67		
863.33413	1	19021.87		
864.33715	1	9170.11		

Formula Calculator Results

Formula	Best	Mass	Tgt Mass	Diff (ppm)	Ion Species	Score
C22 H24 N6 O S	TRUE	420.17334	420.17323	-0.27	C22 H25 N6 O S	87.67

Figure S26. HRMS Qualitative analaysis of H1

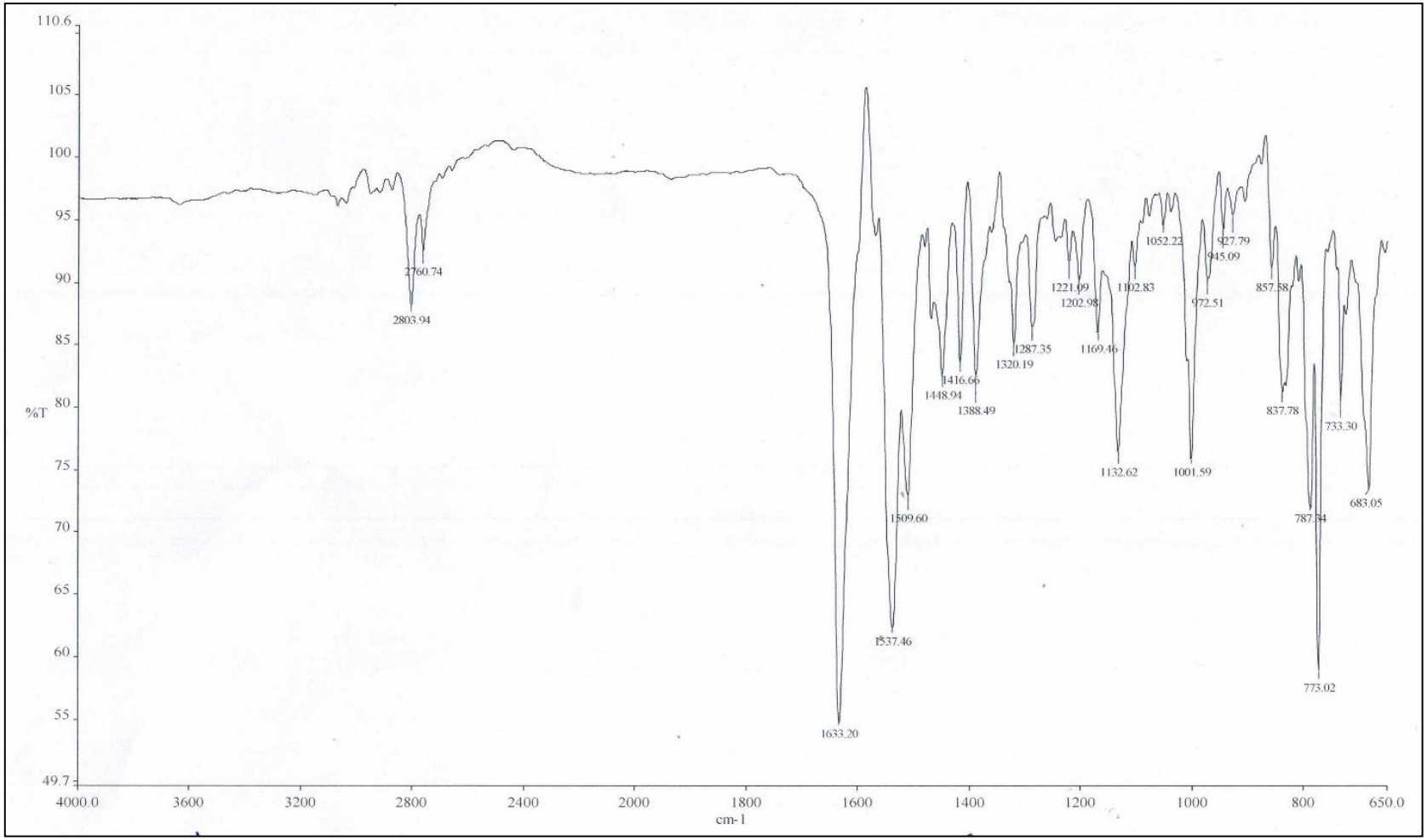


Figure S27. IR Spectra of H2

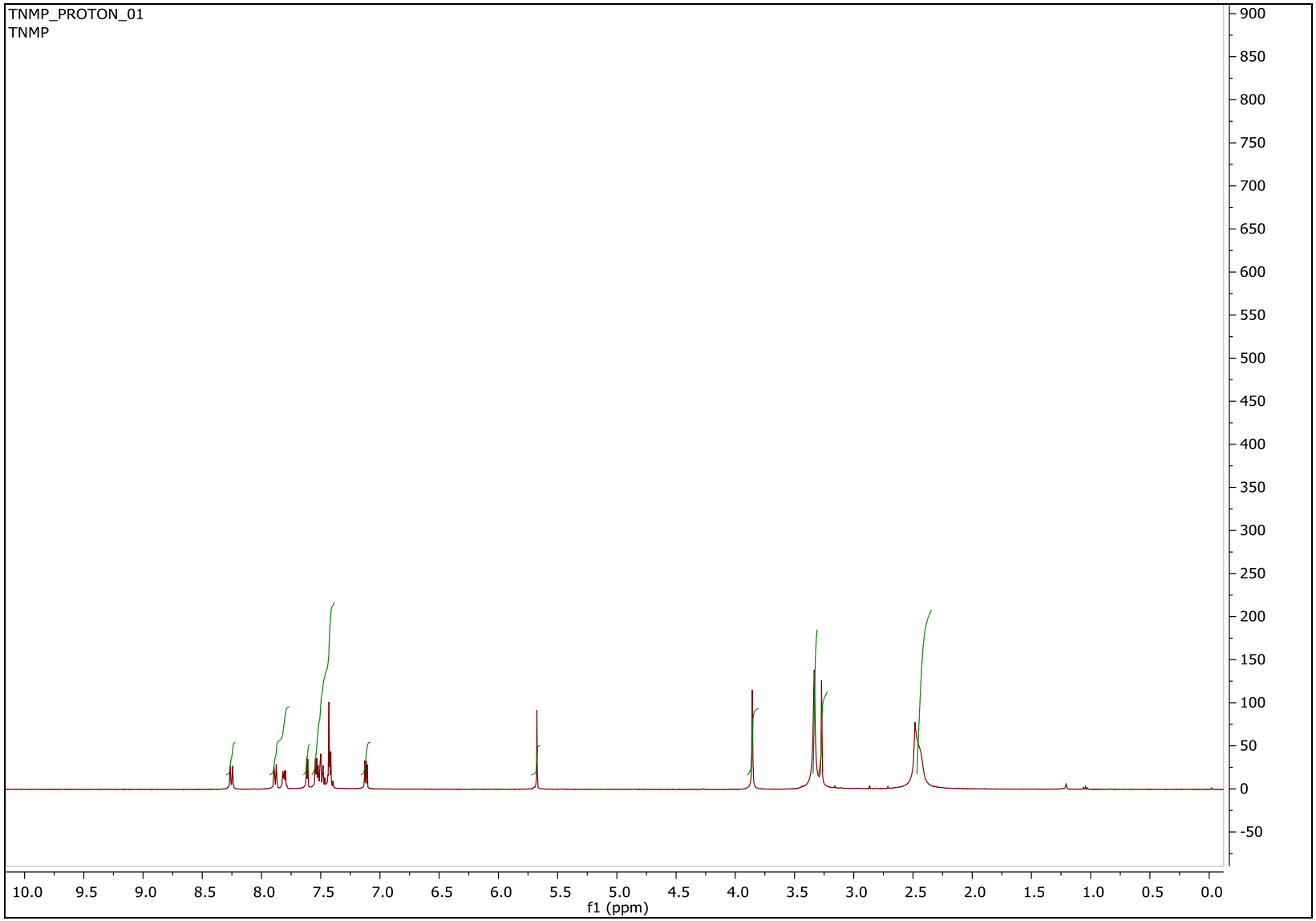


Figure S28. ^{1}H NMR spectra of H2

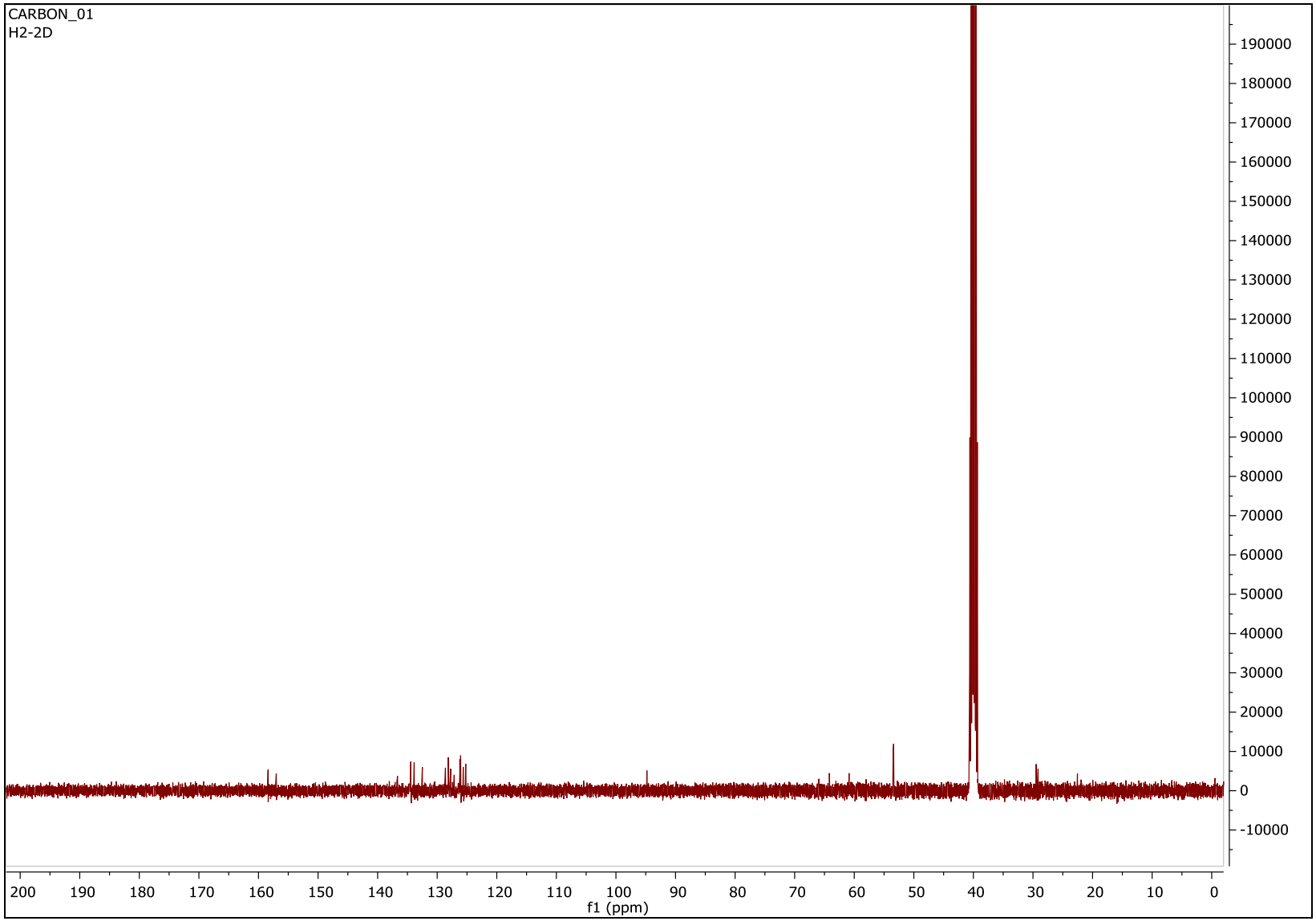


Figure S29. ^{13}C NMR Spectra of H2

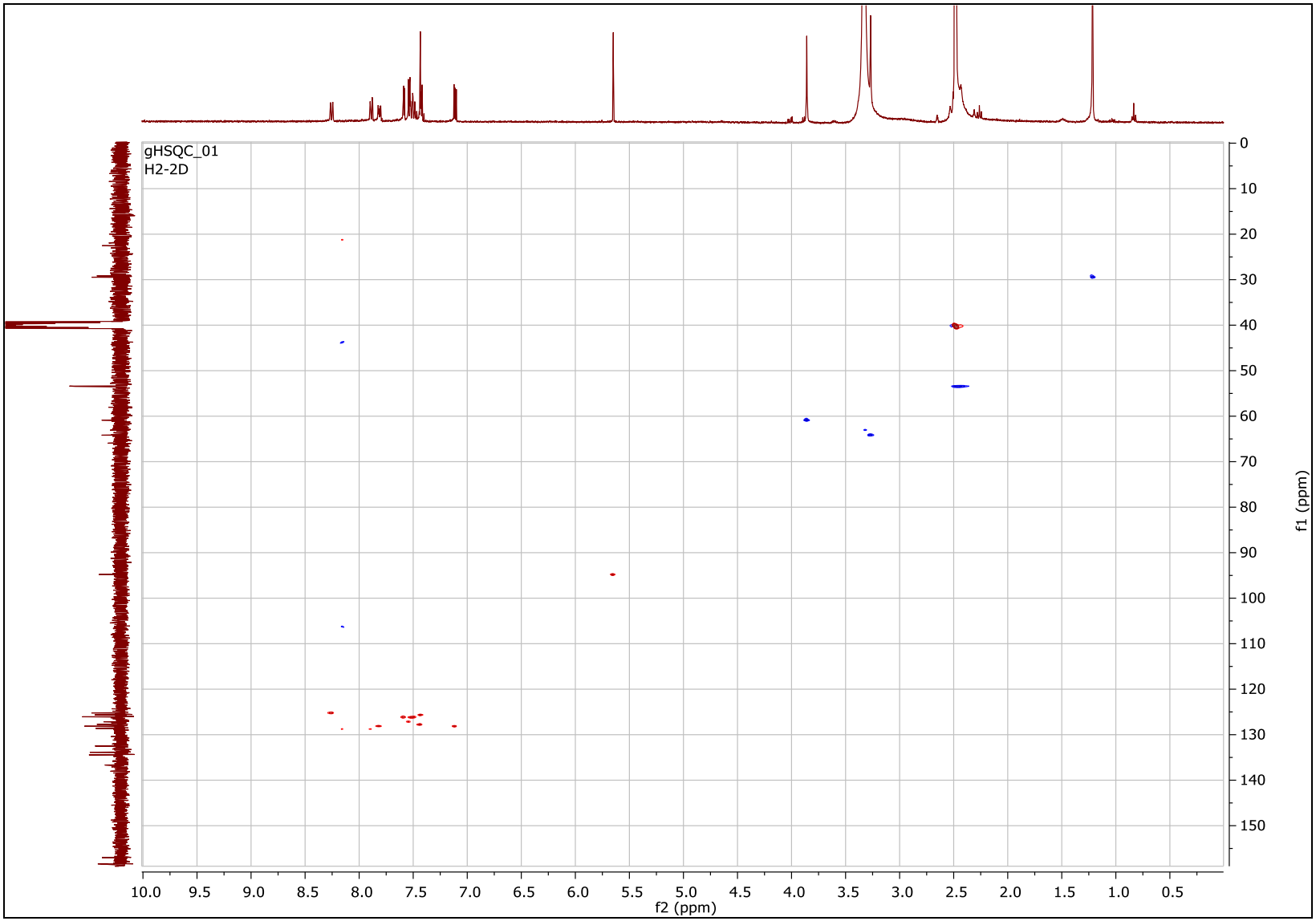


Figure S30. HSQC NMR Spectra of H2

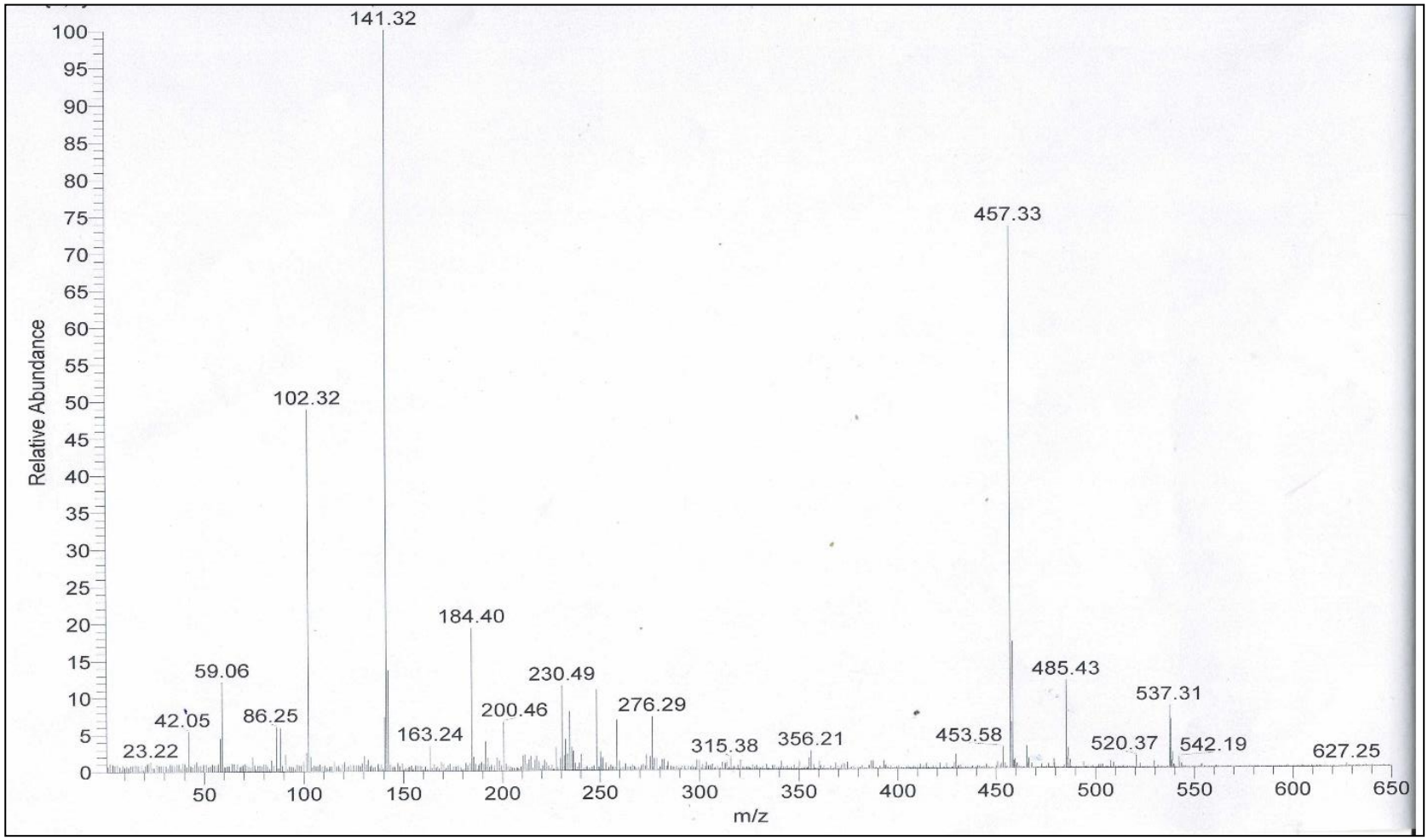


Figure S31. Mass spectra of H2

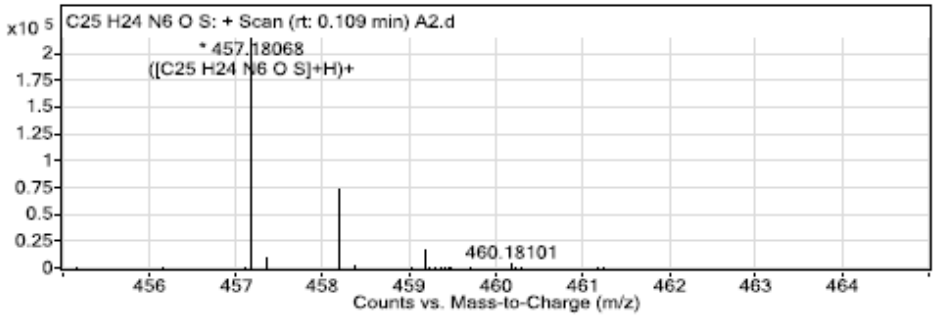
Qualitative Analysis Report

Data Filename	A2.d	**Sample Name**	A2
Sample Type	Sample	**Position**	P1-C3
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI pos.m	**Acquired Time**	2/17/2020 3:40:40 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.08.00 (B8058.0)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
90	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
121.04966	1	24739.37		
132.9035		11138.31		
141.06848	1	36230.61		
227.15207	1	10298.35		
293.17332	1	13335.52		
317.11638	1	33988.92		
457.18068	1	213136.63	C25 H24 N6 O S	(M+H)+
457.36313	1	10305.4		
458.18258	1	73550.02	C25 H24 N6 O S	(M+H)+
459.18025	1	17180.29	C25 H24 N6 O S	(M+H)+
479.16148	1	12157.13		
589.07725	1	80423.84		
590.08091	1	22016.81		
683.32599	1	11022.35		
913.35349	1	161885		
914.35646	1	103200.01		
915.3557	1	37806.87		
916.35617	1	13071.06		
935.33566	1	34084.59		
936.336	1	20414.57		

Formula Calculator Results

Formula	Best	Mass	Tgt Mass	Diff (ppm)	Ion Species	Score
C25 H24 N6 O S	TRUE	456.17311	456.17323	0.26	C25 H25 N6 O S	94.27

Figure S32. HRMS Qualitative analysis of H2

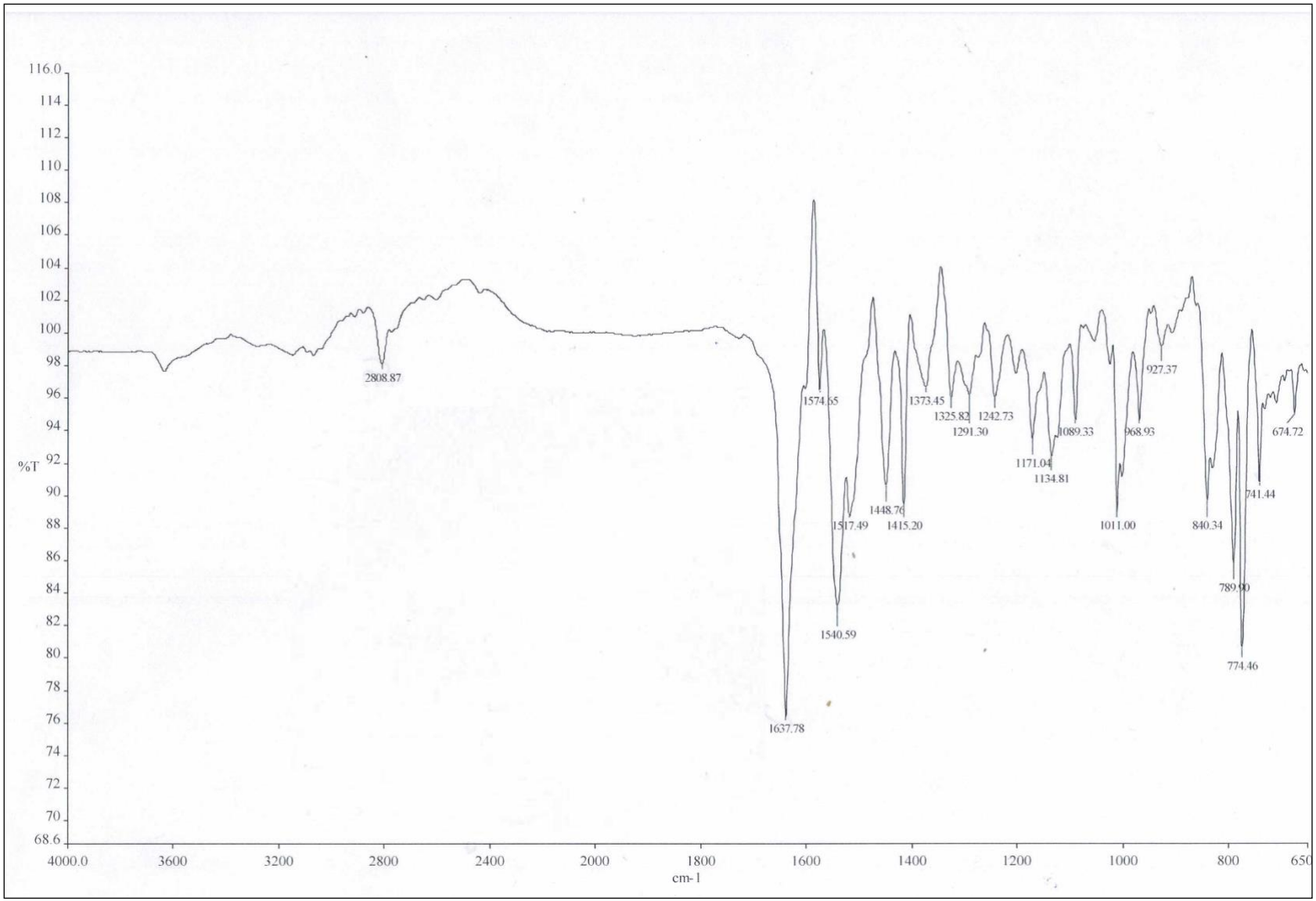


Figure S33. IR spectra of H3

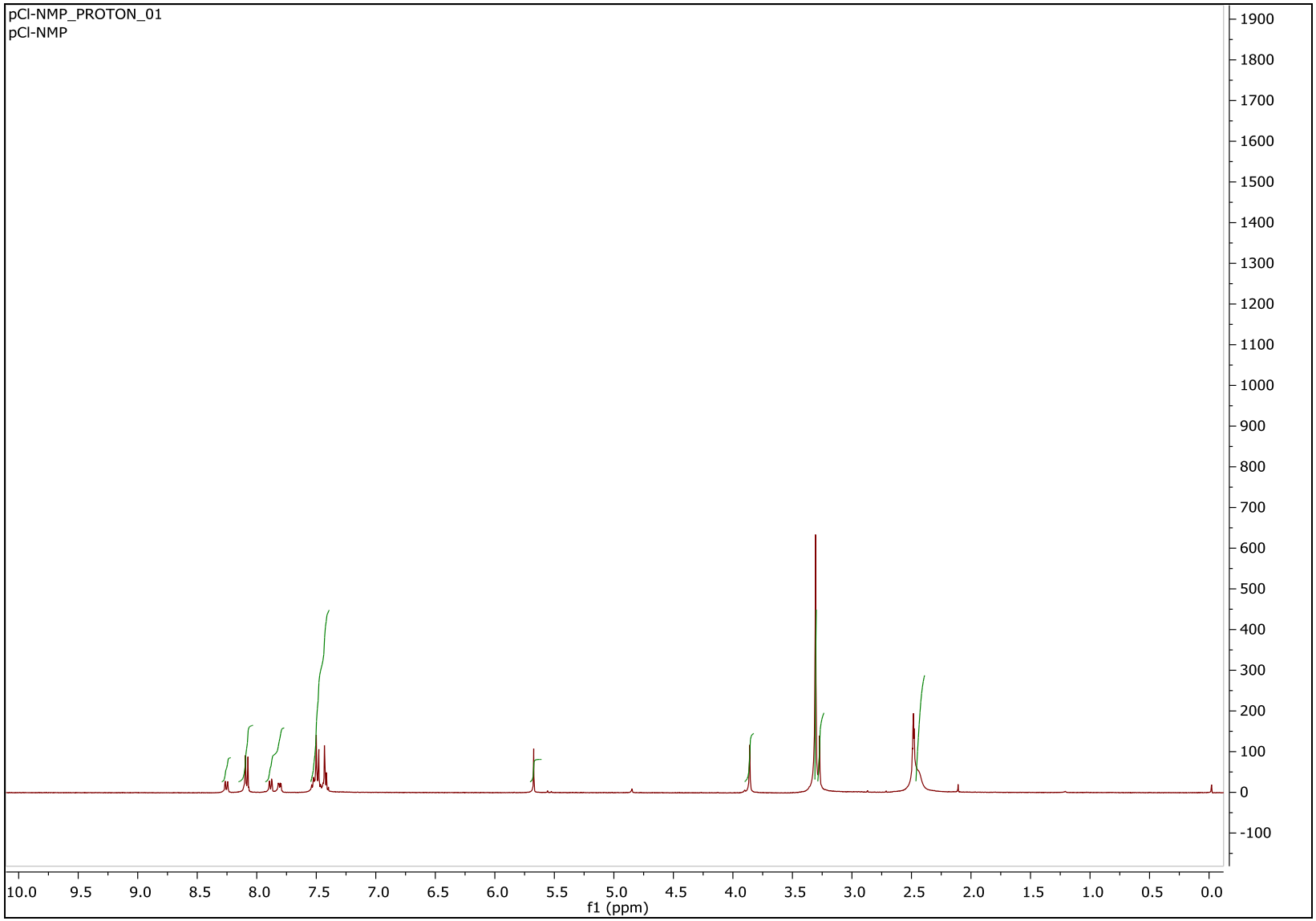


Figure S34. ^{1}H NMR Spectra of H3

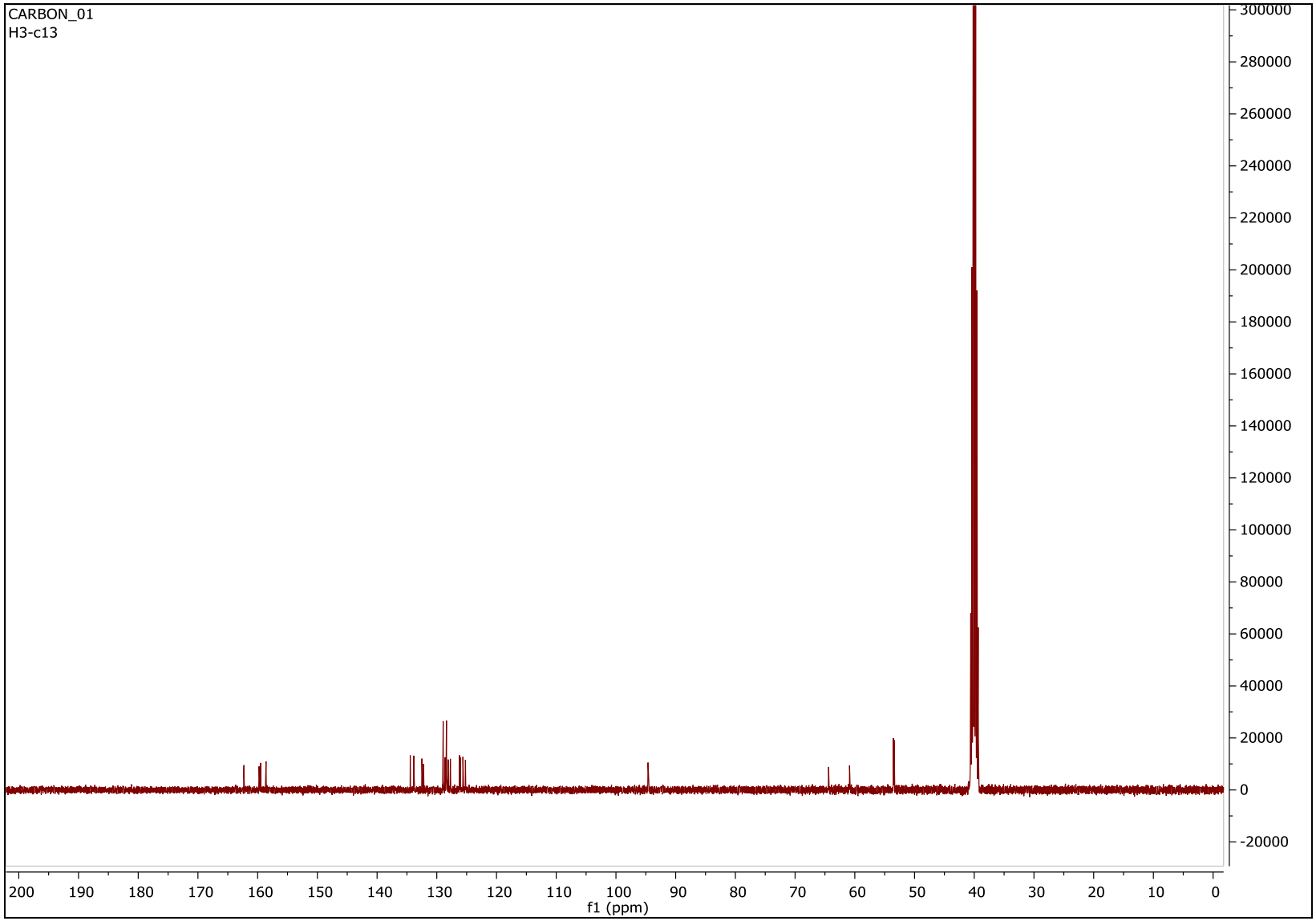


Figure S35. ^{13}C NMR Spectra of H3

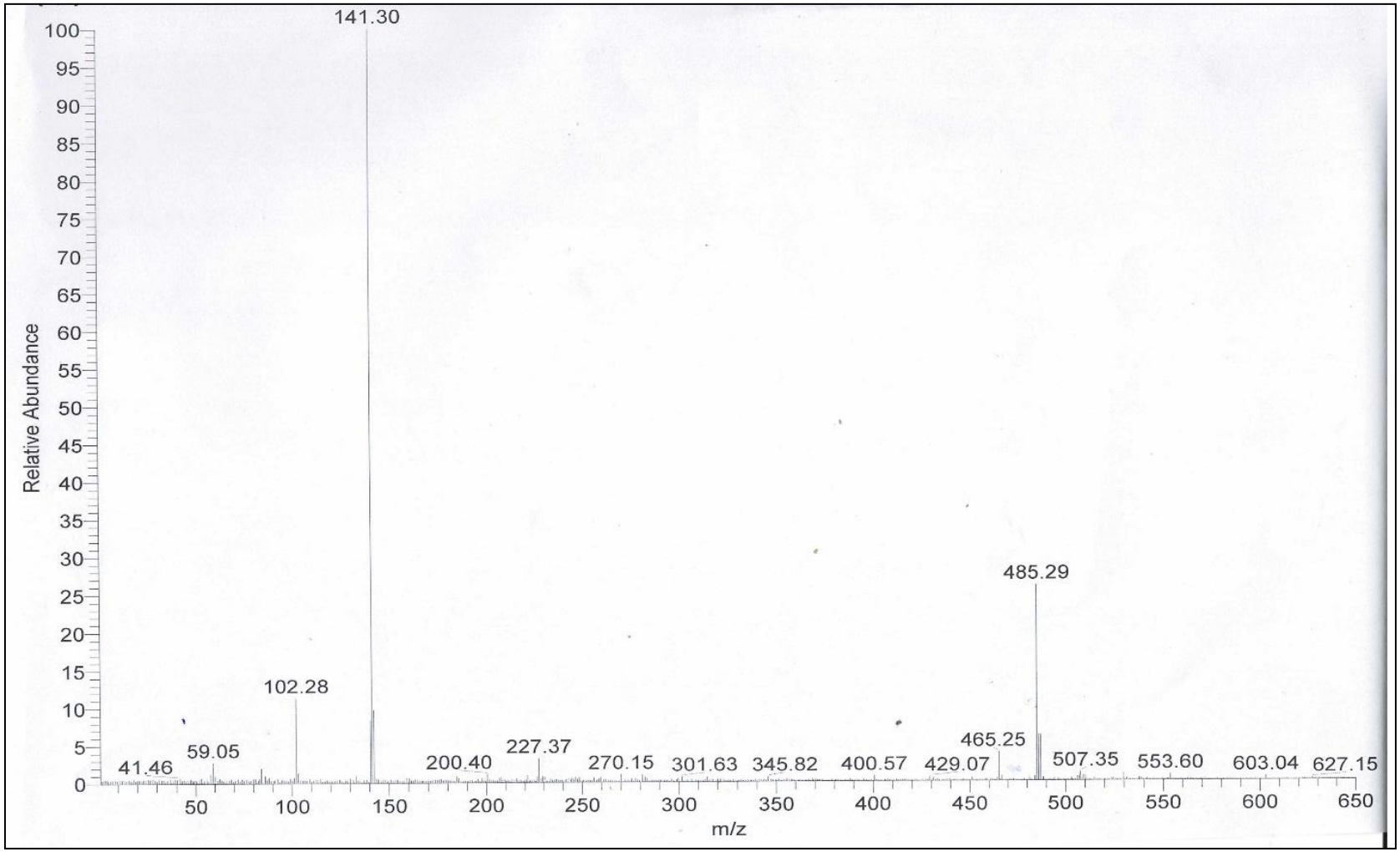


Figure S36. Mass spectra of H3

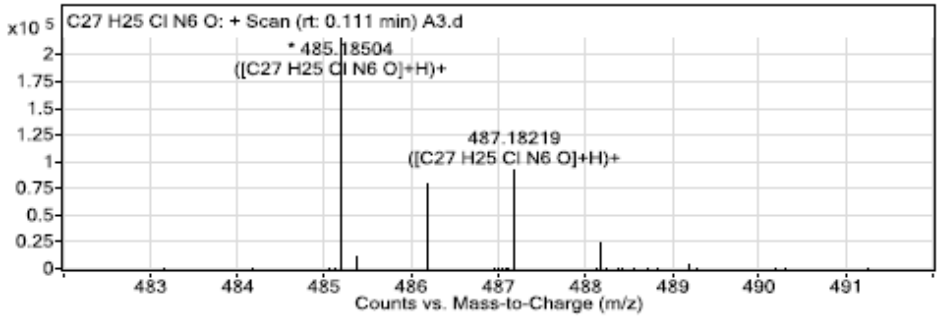
Qualitative Analysis Report

Data Filename	A3.d	**Sample Name**	A3
Sample Type	Sample	**Position**	P1-C4
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI pos.m	**Acquired Time**	2/17/2020 3:43:22 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.08.00 (B8058.0)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
90	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
121.04974	1	20774.08		
132.90292		18682.23		
141.06808	1	33554.56		
227.15209	1	22378.09		
293.17279	1	12979.62		
345.12158	1	20384.21		
485.18504	1	214857.97	C27 H25 Cl N6 O	(M+H)+
486.1874	1	79300.02	C27 H25 Cl N6 O	(M+H)+
487.18219	1	92802.18	C27 H25 Cl N6 O	(M+H)+
488.18514	1	24246.04	C27 H25 Cl N6 O	(M+H)+
501.17887	1	16714.78		
617.08154	1	65145.09		
618.08398	1	19045.03		
619.07999	1	21367.85		
969.36281	1	71922.87		
970.36515	1	43946.38		
971.36127	1	60436.14		
972.36225	1	29519.21		
973.36063	1	13869.57		
991.34308	1	13361.07		

Formula Calculator Results

Formula	Best	Mass	Tgt Mass	Diff (ppm)	Ion Species	Score
C27 H25 Cl N6 O	TRUE	484.17737	484.17784	0.97	C27 H26 Cl N6 O	95.77

Figure S37. HRMS Qualitative analysis of H3

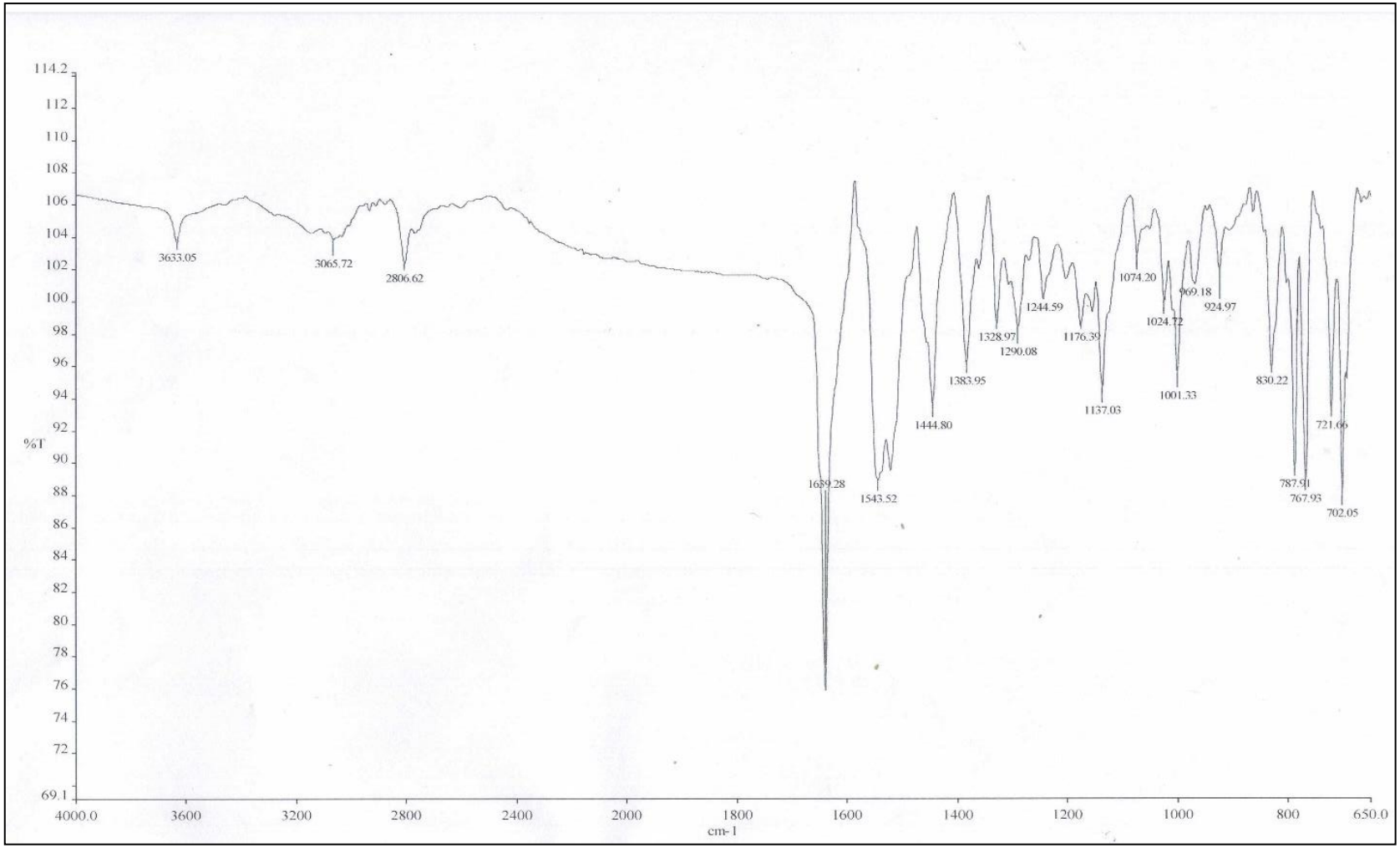


Figure S38. IR spectra of H4

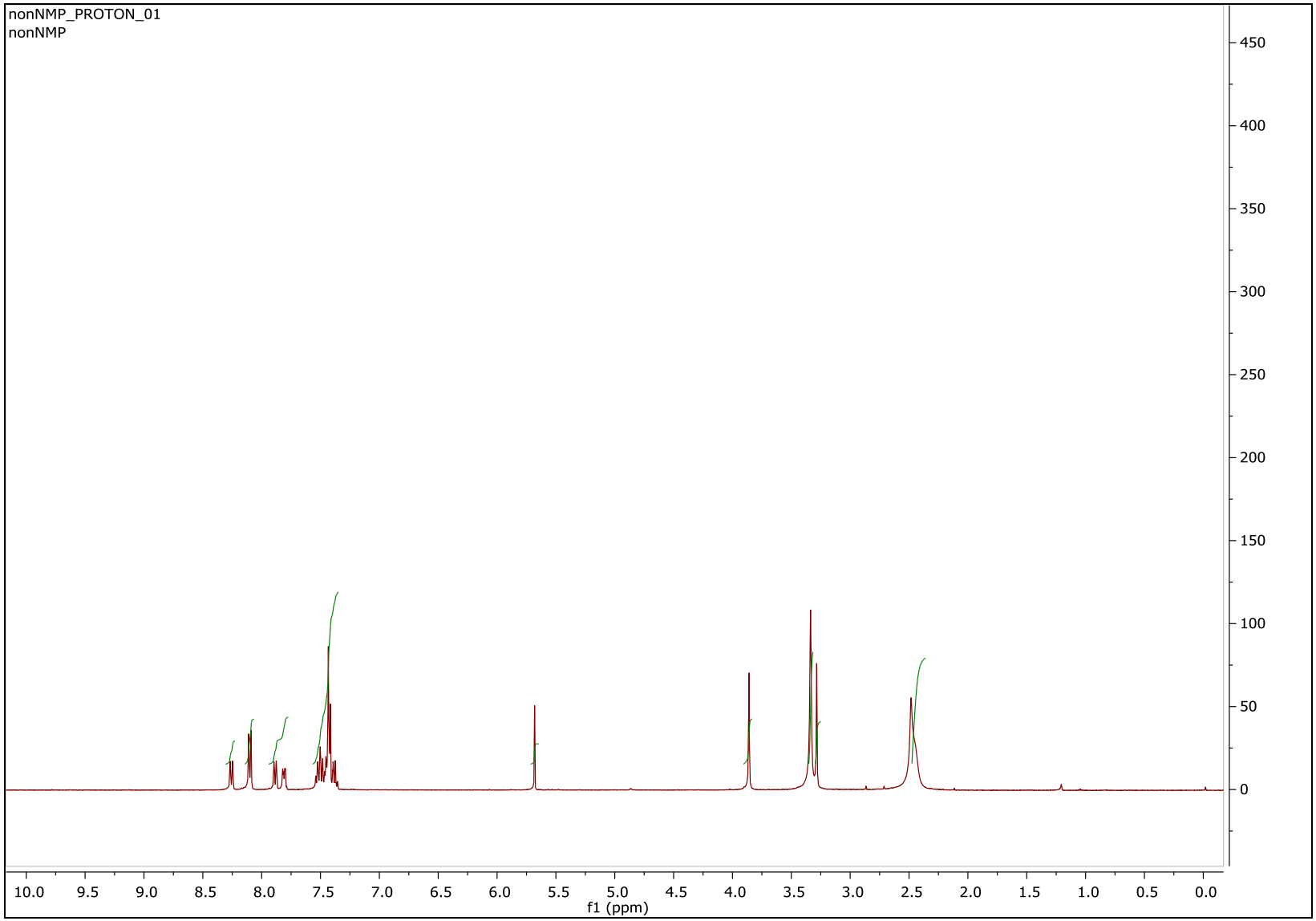


Figure S39. ^{1}H NMR spectra of H4

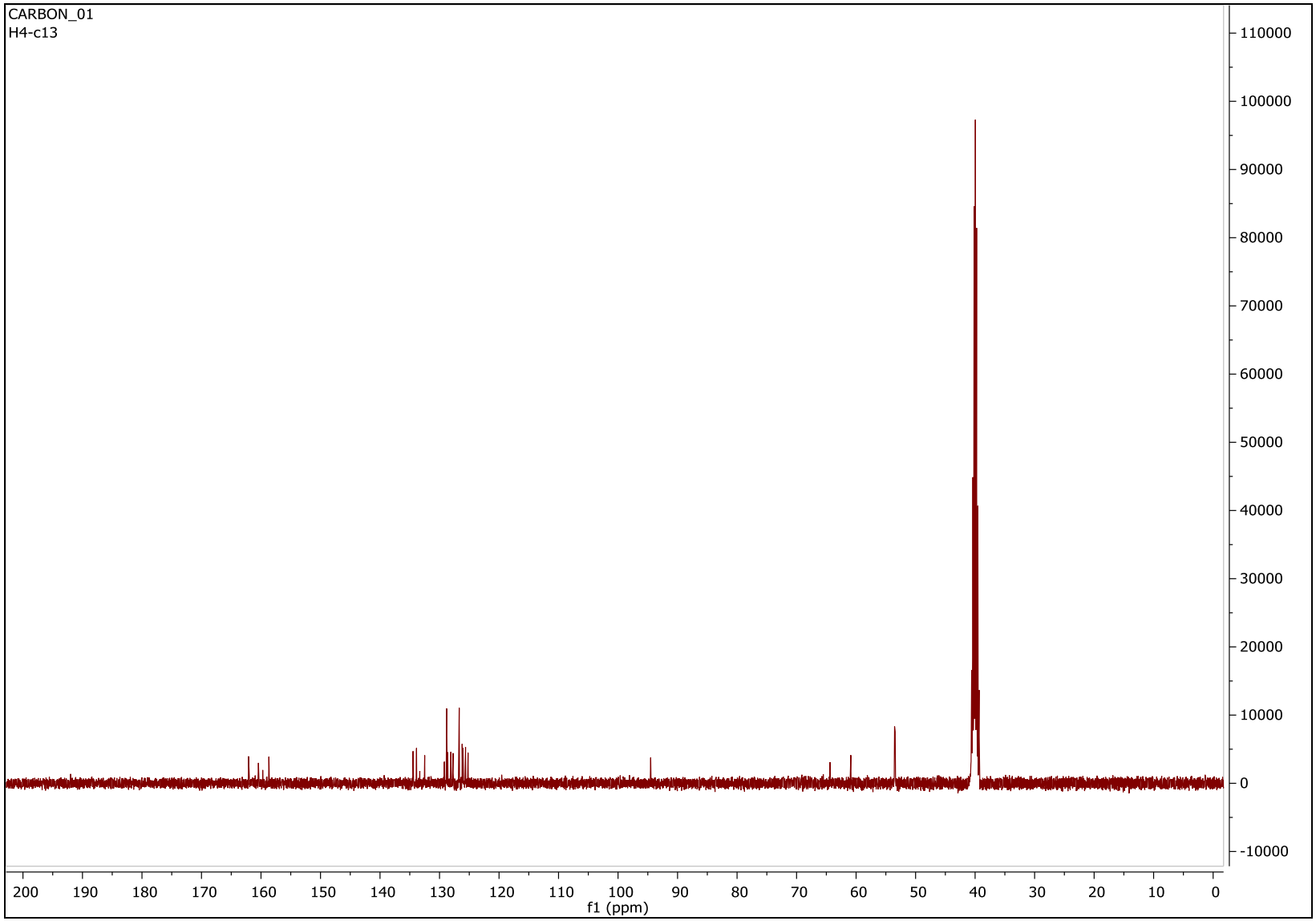


Figure S40. ^{13}C NMR Spectra of H4

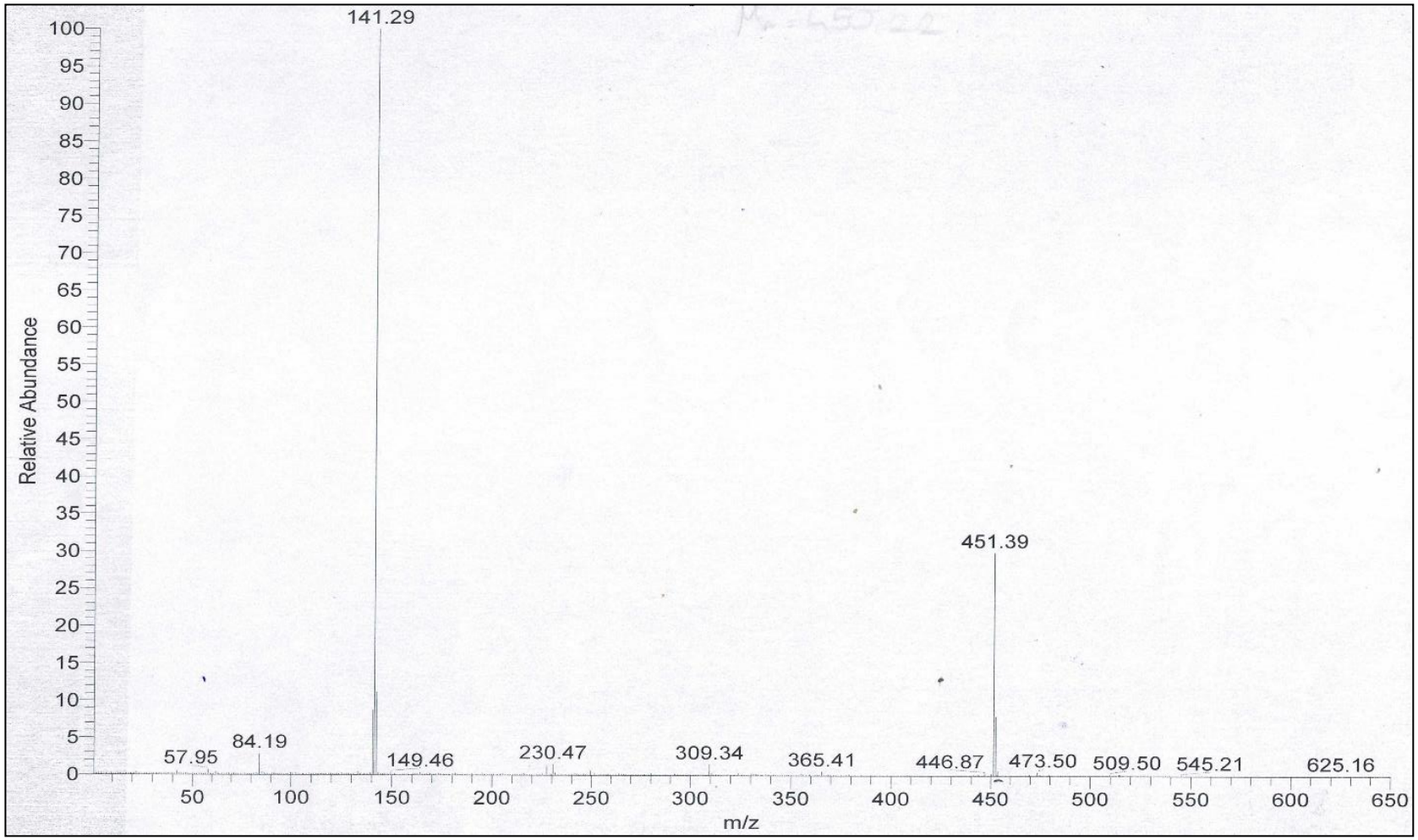


Figure S41. Mass specra of H4

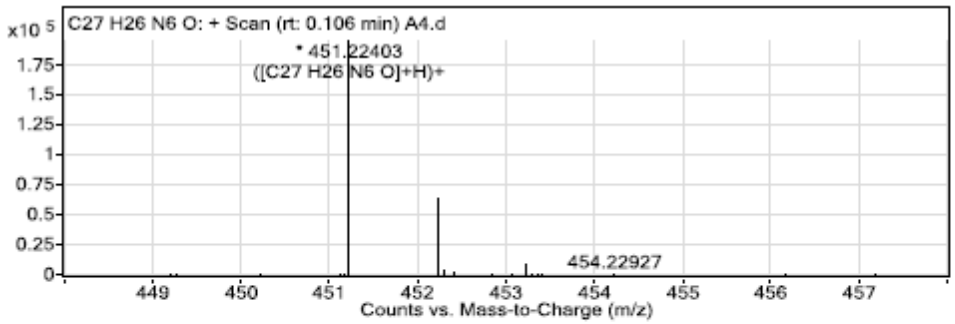
Qualitative Analysis Report

Data Filename	A4.d	**Sample Name**	A4
Sample Type	Sample	**Position**	P1-C5
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI pos.m	**Acquired Time**	2/17/2020 3:46:05 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.08.00 (B8058.0)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
90	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
102.09054		14621.21		
121.04989	1	20970.71		
141.06805	1	46220.82		
142.12164		7758.49		
293.17281	1	13646.75		
311.16033	1	44645.86		
451.22403	1	194630	C27 H26 N6 O	(M+H)+
452.22551	1	64371.82	C27 H26 N6 O	(M+H)+
453.22876	1	8143.25	C27 H26 N6 O	(M+H)+
467.2167	1	9496.47		
473.20496	1	19108.98		
583.1207	1	30049.97		
584.12438	1	9348.68		
901.44135	1	133231.61		
902.4437	1	81813.52		
903.44611	1	22897.8		
923.42295	1	61748.57		
924.42593	1	37485.32		
925.42826	1	12068.61		
939.40136	1	7709.12		

Formula Calculator Results

Formula	Best	Mass	Tgt Mass	Diff (ppm)	Ion Species	Score
C27 H26 N6 O	TRUE	450.21637	450.21681	0.99	C27 H27 N6 O	96.85

Figure S42. HRMS Qualitative analysis of H4

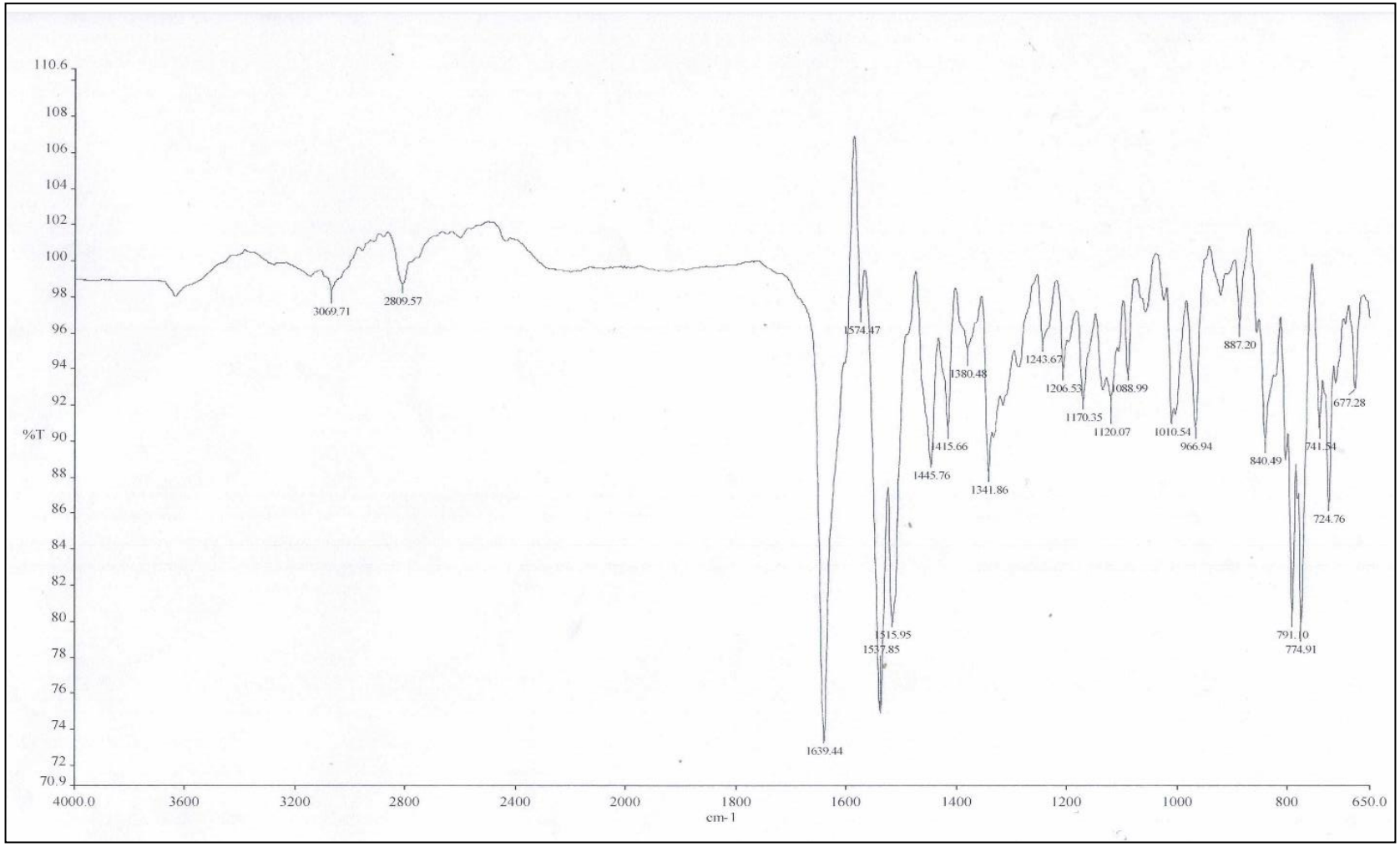


Figure S43. IR spectra of H5

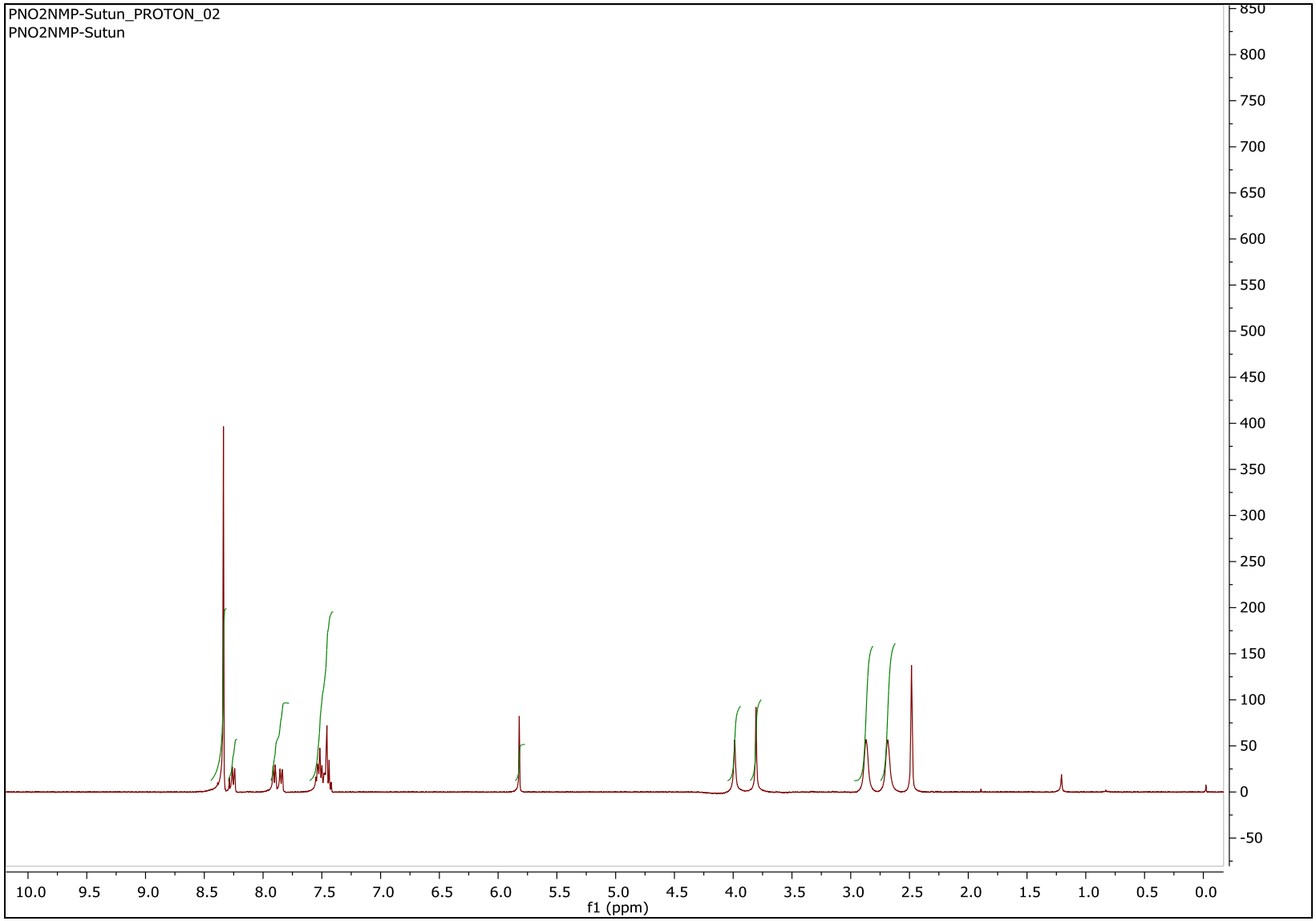


Figure S44. ^{1}H NMR spectra of H5

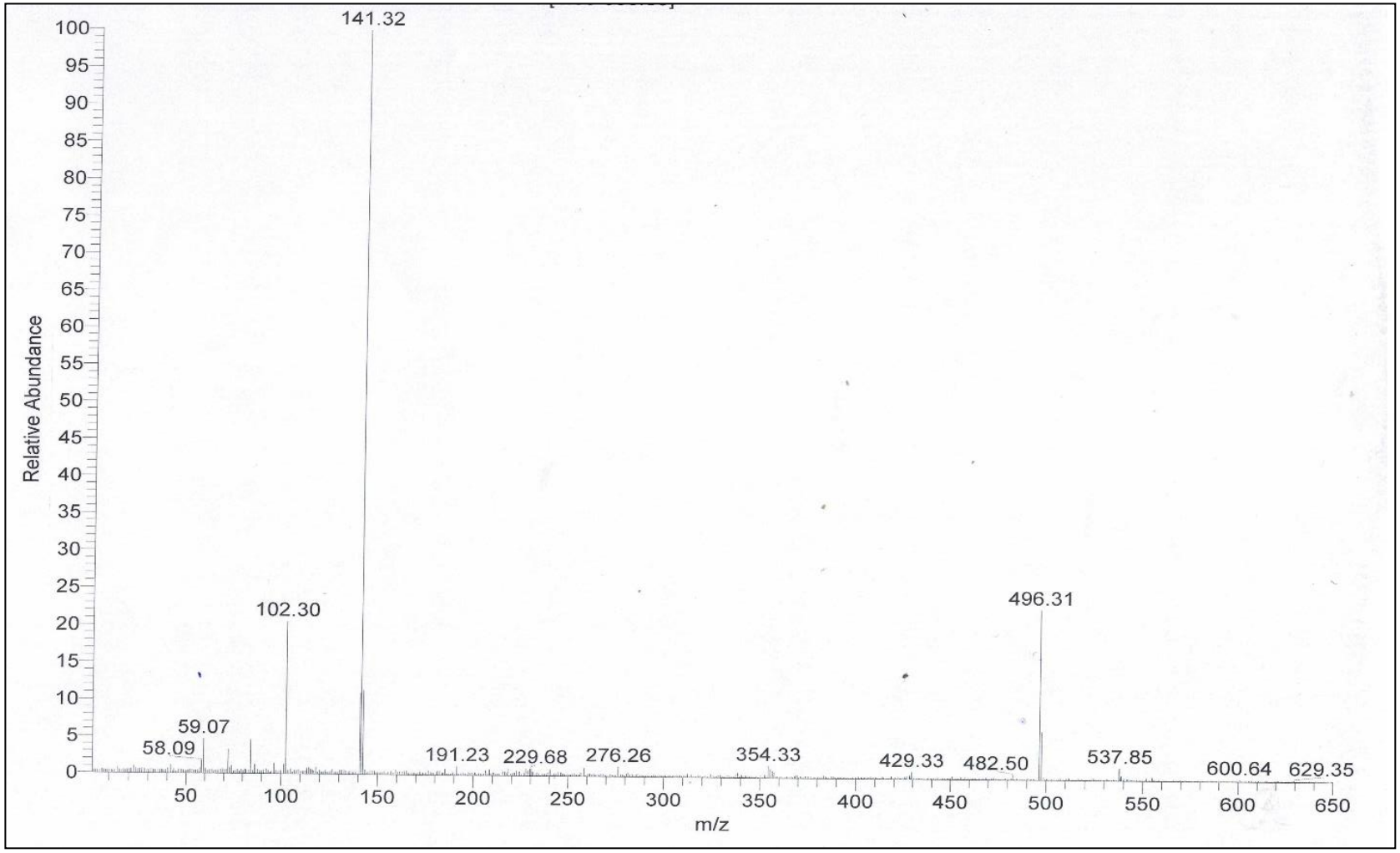


Figure S45. Mass spectra of H5

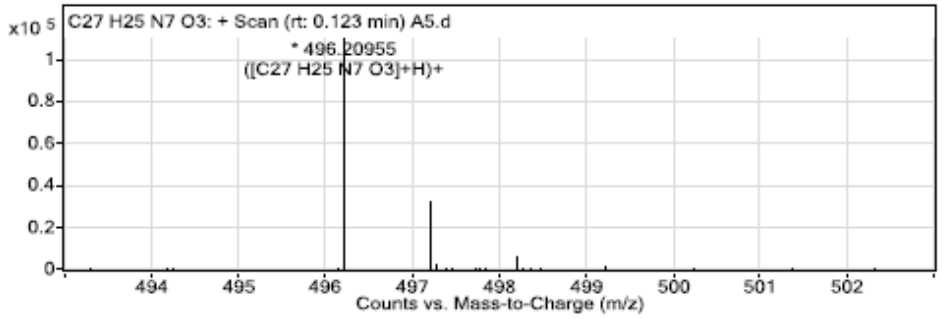
Qualitative Analysis Report

Data Filename	A5.d	**Sample Name**	A5
Sample Type	Sample	**Position**	P1-C6
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI pos.m	**Acquired Time**	2/17/2020 3:48:47 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.08.00 (B8058.0)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
90	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
100.07511	1	154093.63		
101.07846	1	9166.72		
121.04978		9792.38		
151.09508	1	23813.46		
168.12129		8926.29		
173.07682	1	128003.78		
199.14251	1	19983.87		
202.17862	1	42523.62		
217.10297	1	41579.47		
227.1524	1	8997.39		
274.27291	1	9737.49		
288.28849	1	27331.15		
316.32005	1	12103.47		
338.34046	1	26460		
449.26899	1	19965.62		
496.20955	1	109366.19	C27 H25 N7 O3	(M+H)+
497.21143	1	31952.09	C27 H25 N7 O3	(M+H)+
554.55097	1	17433.93		
582.57988	1	8792.14		
991.4112	1	7982.1		

Formula Calculator Results

Formula	Best	Mass	Tgt Mass	Diff (ppm)	Ion Species	Score
C27 H25 N7 O3	TRUE	495.20201	495.20189	-0.26	C27 H26 N7 O3	97.76

Figure S46. HRMS Qualitative analysis of H5

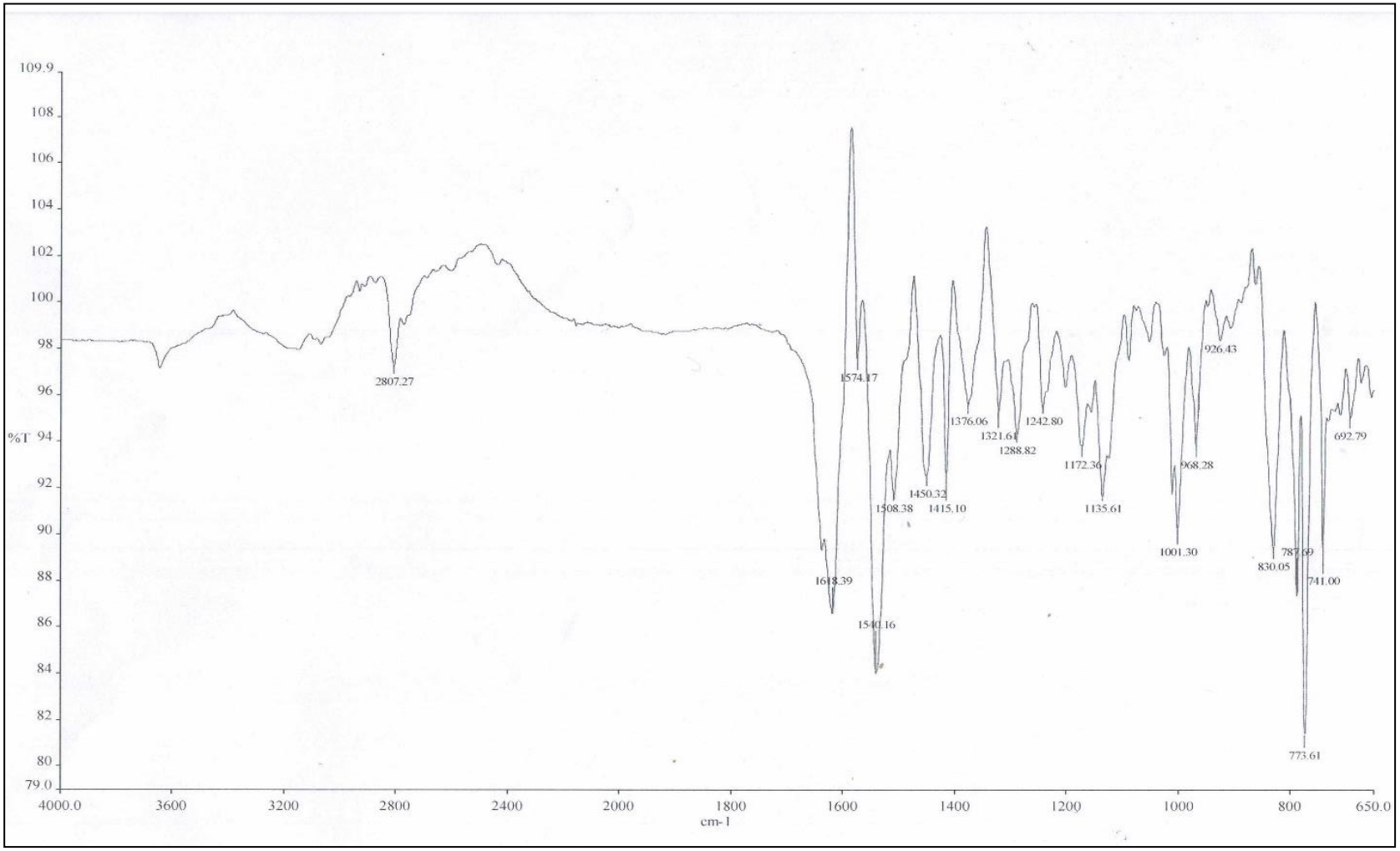


Figure S47. IR spectra of H6

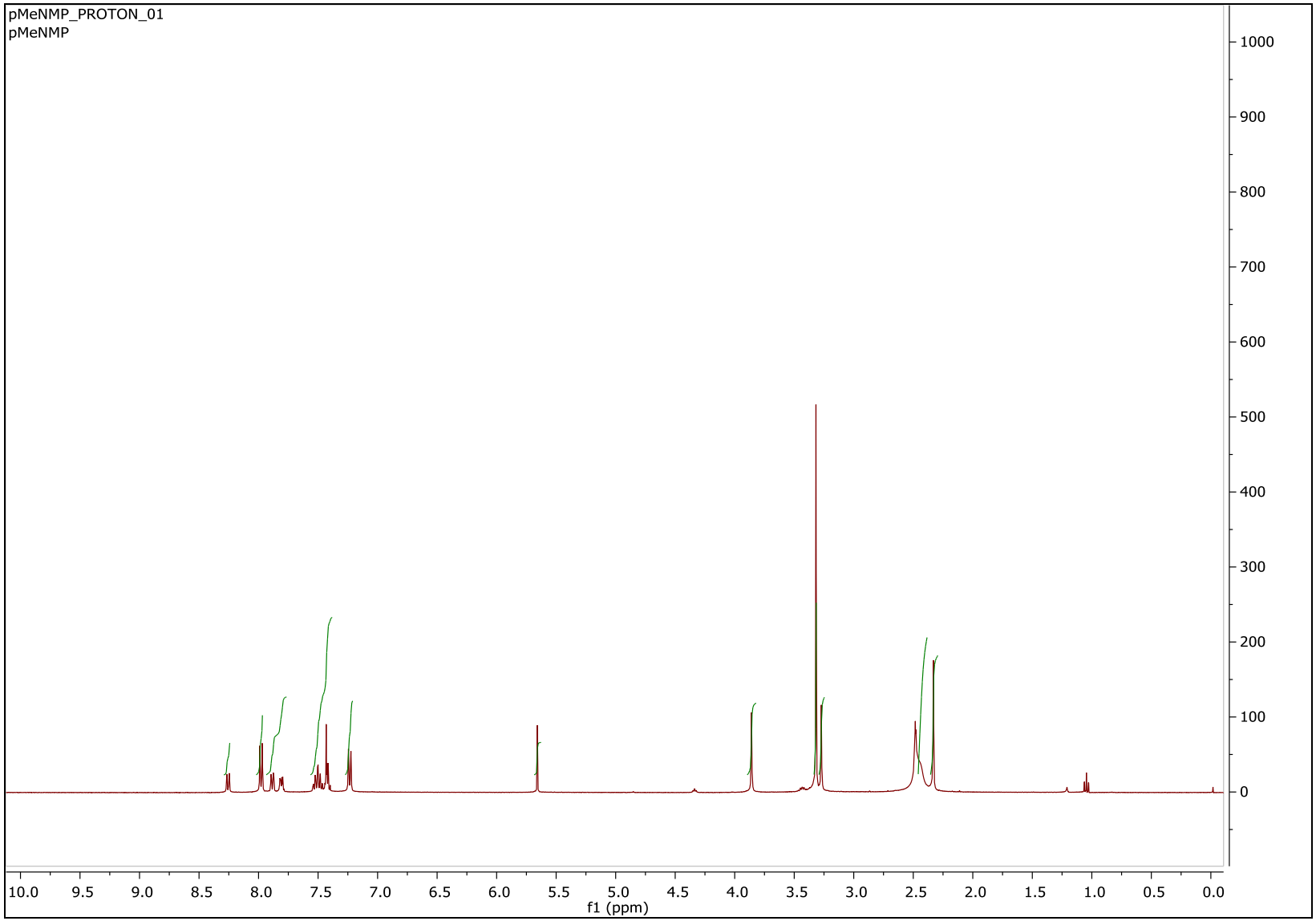


Figure S48. ^{1}H NMR spectra of H6

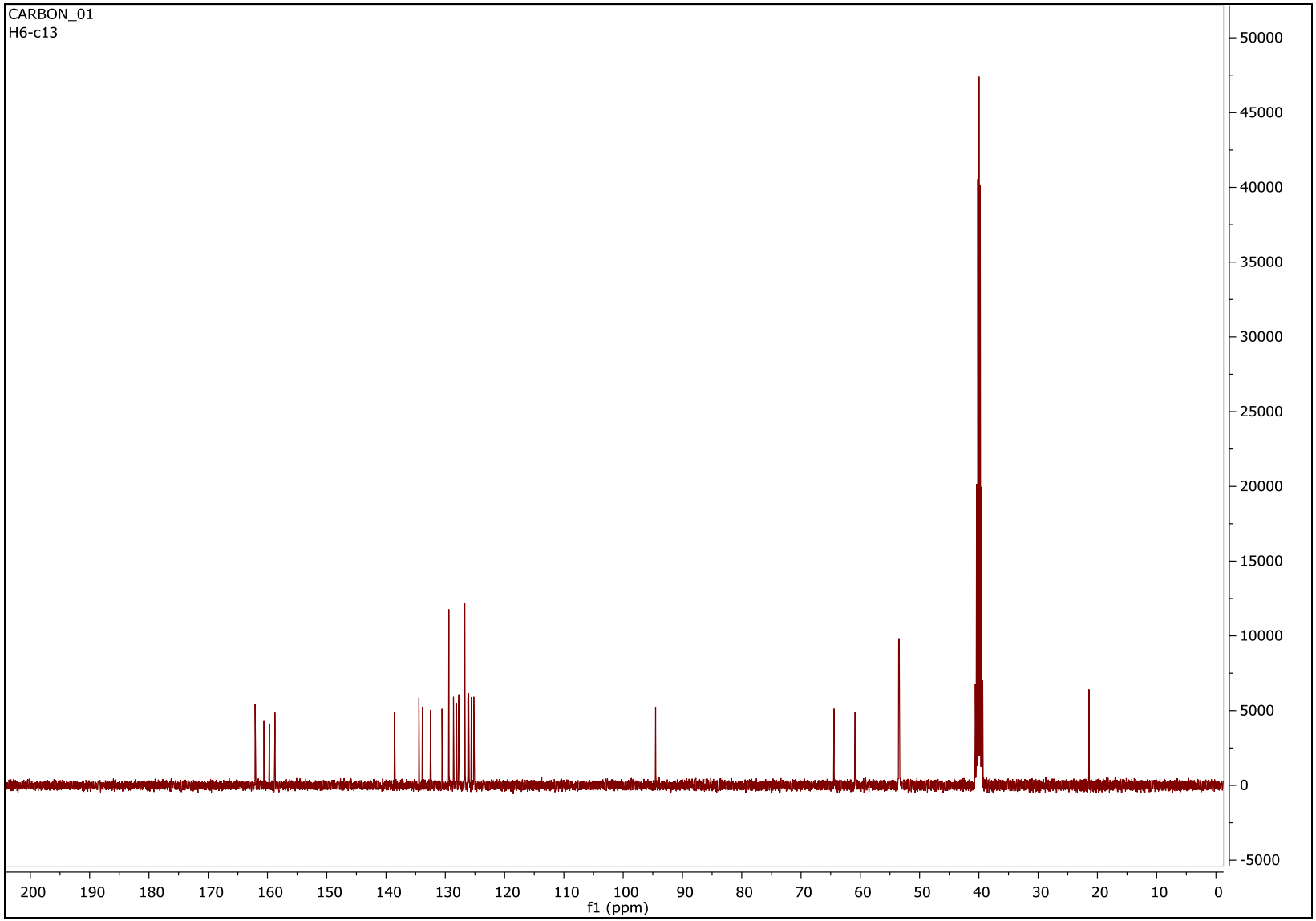


Figure S49. ^{13}C NMR Spectra of H6

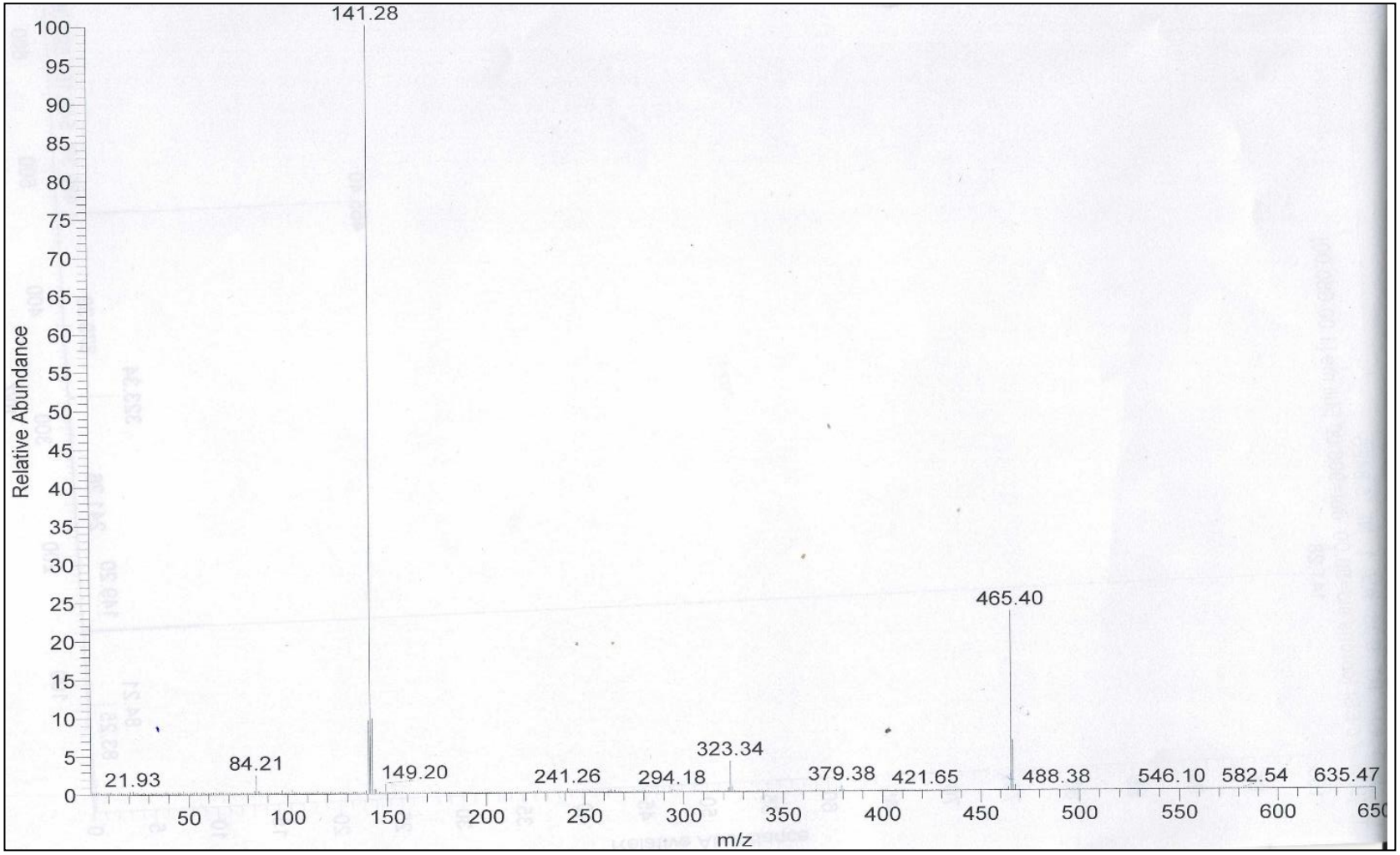


Figure S50. Mass spectra of H6

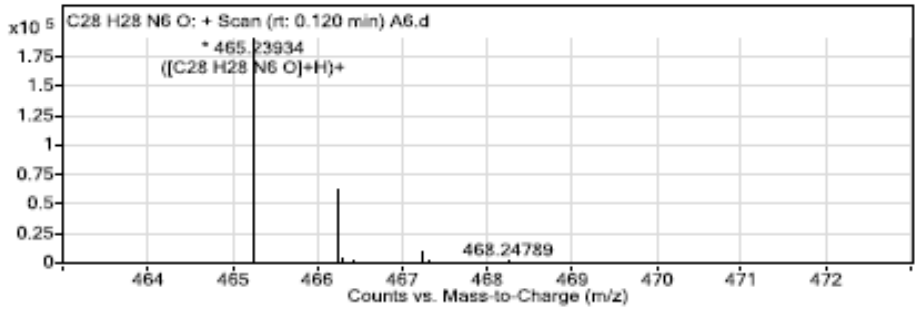
Qualitative Analysis Report

Data Filename	A6.d	**Sample Name**	A6
Sample Type	Sample	**Position**	P1-C7
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI pos.m	**Acquired Time**	2/17/2020 3:51:29 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.08.00 (B8058.0)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
90	0	ESI



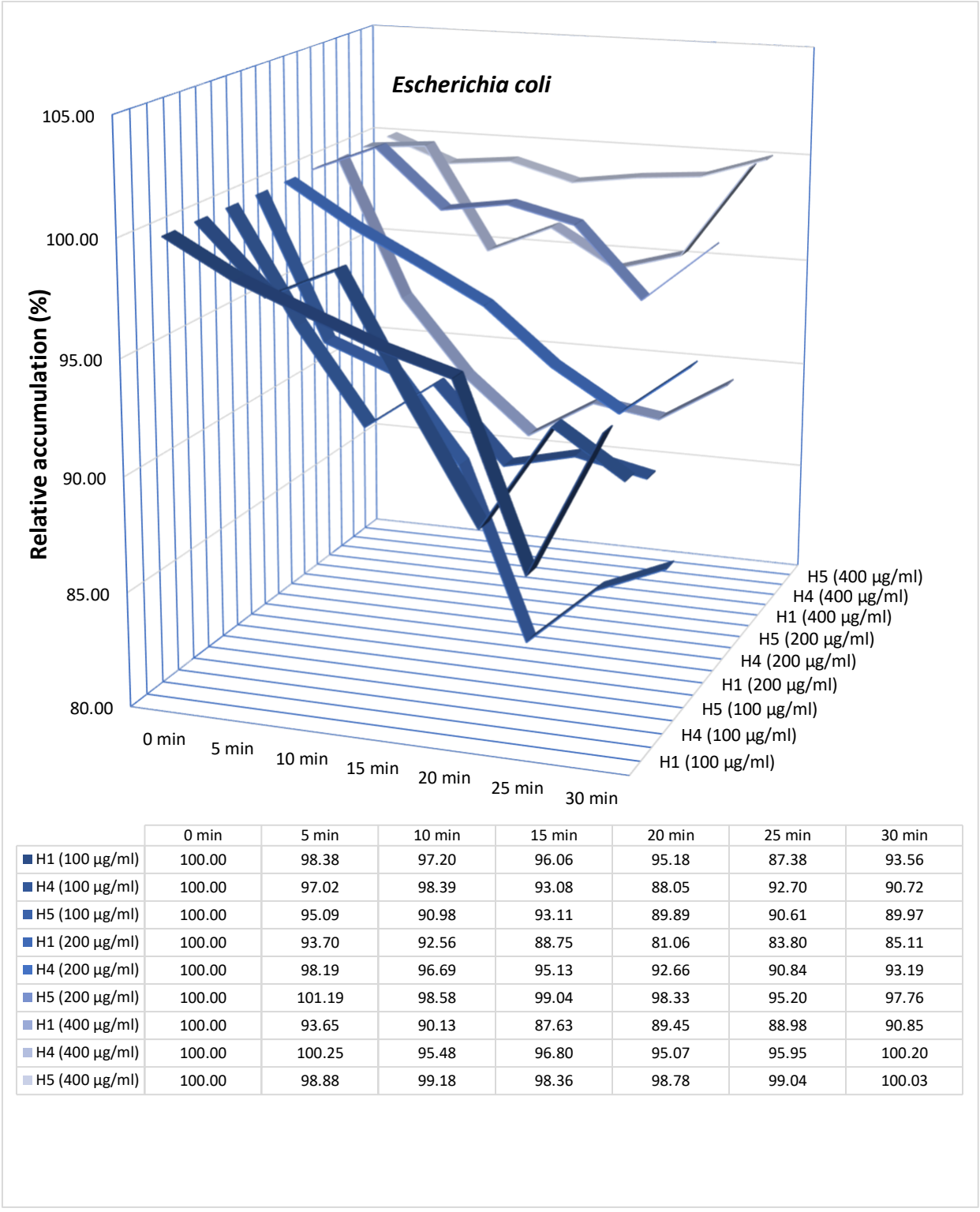
Peak List

m/z	z	Abund	Formula	Ion
121.04984	1	23779.42		
132.90267		11735.14		
141.06878	1	19123.42		
141.11108		4132.77		
233.12109	2	4261.21		
279.09084	1	6294.31		
293.17307	1	15091		
325.17569	1	18869.59		
465.23934	1	190355.28	C28 H28 N6 O	(M+H)+
466.24145	1	61900.37	C28 H28 N6 O	(M+H)+
467.24363	1	8237.59	C28 H28 N6 O	(M+H)+
597.13711	1	194012.19		
598.13918	1	61725.08		
599.14115	1	9151.64		
929.47213	1	119054.76		
930.47497	1	72965.77		
931.47824	1	22277.24		
932.47649	1	4981.84		
951.45607	1	6741.21		
952.45446	1	4375.55		

Formula Calculator Results

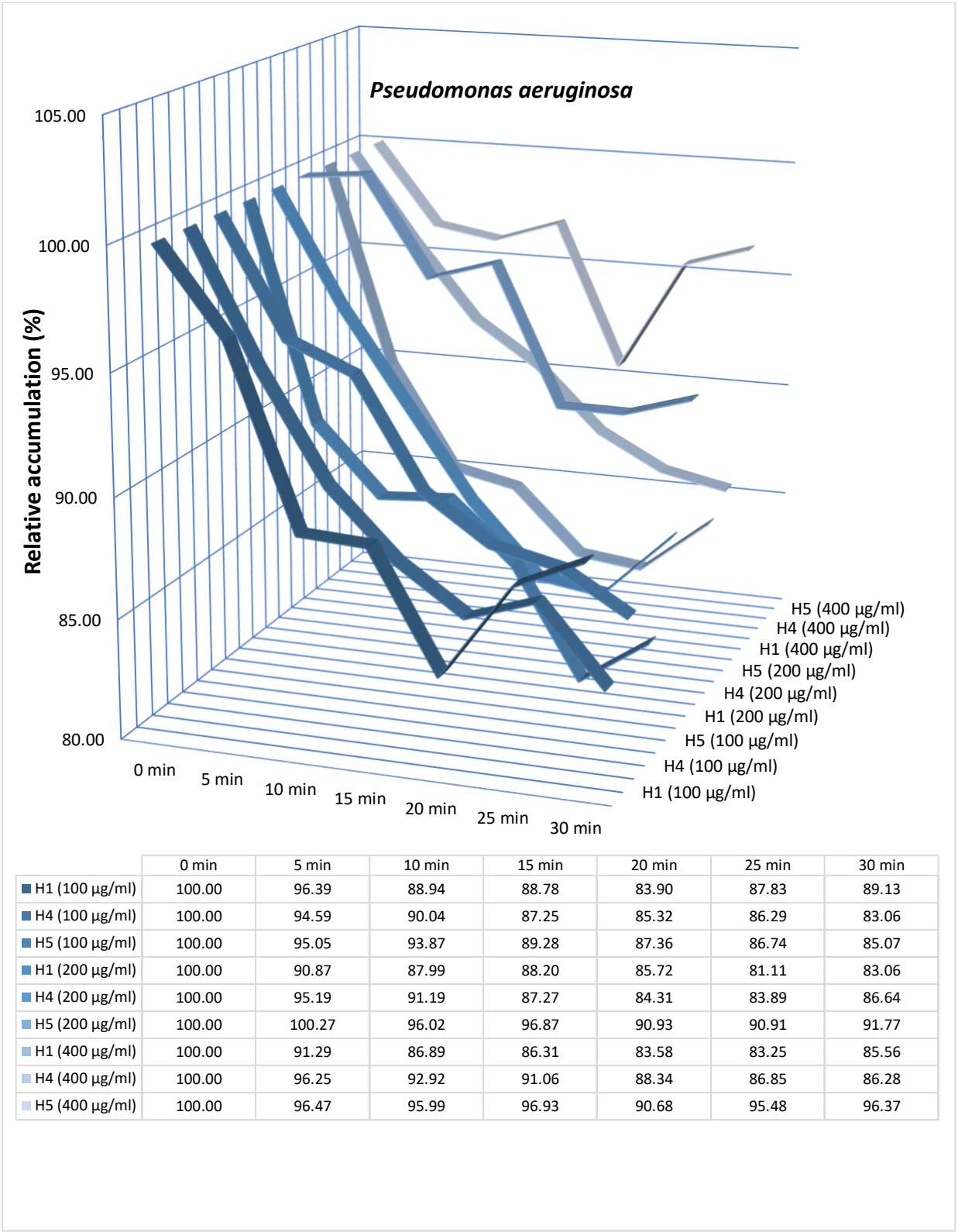
Formula	Best	Mass	Tgt Mass	Diff (ppm)	Ion Species	Score
C28 H28 N6 O	TRUE	464.23181	464.23246	1.39	C28 H29 N6 O	97.86

Figure S51. HRMS Qualitative analysis of H



	0 min	5 min	10 min	15 min	20 min	25 min	30 min
H1 (100 µg/ml)	100.00	98.38	97.20	96.06	95.18	87.38	93.56
H4 (100 µg/ml)	100.00	97.02	98.39	93.08	88.05	92.70	90.72
H5 (100 µg/ml)	100.00	95.09	90.98	93.11	89.89	90.61	89.97
H1 (200 µg/ml)	100.00	93.70	92.56	88.75	81.06	83.80	85.11
H4 (200 µg/ml)	100.00	98.19	96.69	95.13	92.66	90.84	93.19
H5 (200 µg/ml)	100.00	101.19	98.58	99.04	98.33	95.20	97.76
H1 (400 µg/ml)	100.00	93.65	90.13	87.63	89.45	88.98	90.85
H4 (400 µg/ml)	100.00	100.25	95.48	96.80	95.07	95.95	100.20
H5 (400 µg/ml)	100.00	98.88	99.18	98.36	98.78	99.04	100.03

Figure S52. Effects of the compounds on ethidium bromide accumulation by *Escherichia coli*



	0 min	5 min	10 min	15 min	20 min	25 min	30 min
H1 (100 µg/ml)	100.00	96.39	88.94	88.78	83.90	87.83	89.13
H4 (100 µg/ml)	100.00	94.59	90.04	87.25	85.32	86.29	83.06
H5 (100 µg/ml)	100.00	95.05	93.87	89.28	87.36	86.74	85.07
H1 (200 µg/ml)	100.00	90.87	87.99	88.20	85.72	81.11	83.06
H4 (200 µg/ml)	100.00	95.19	91.19	87.27	84.31	83.89	86.64
H5 (200 µg/ml)	100.00	100.27	96.02	96.87	90.93	90.91	91.77
H1 (400 µg/ml)	100.00	91.29	86.89	86.31	83.58	83.25	85.56
H4 (400 µg/ml)	100.00	96.25	92.92	91.06	88.34	86.85	86.28
H5 (400 µg/ml)	100.00	96.47	95.99	96.93	90.68	95.48	96.37

Figure S53. Effects of the compounds on ethidium bromide accumulation by *Pseudomonas aeruginosa*